ABSTRACTS OF WORLD MEDICINE

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Hygiene and Public Health

437. **The Care of the Chronic Sick. II. Social and Demographic Data**

C. R. LOWE and T. MCKEOWN. *British Journal of Social Medicine* [*Brit. J. soc. Med.*] **4**, 61–74, April, 1950. 4 figs., 8 refs.

Regional Hospital Boards in Britain are now required to make decisions concerning the location, and also the number, of beds that should be provided for the chronic sick. For the shaping of their policies much more information is required about the numbers and needs of this category.

The authors examined the records of two Birmingham hospitals which draw their patients almost entirely from the city of Birmingham and are the only hospitals for the chronic sick in the city. In one of these the mean duration of stay was found to be 33·2 months, or about fifty times that in the general hospitals. Of the male patients 30%, and of the female patients 36%, had been in hospital for over 3 years; of the 1,005 patients 90% were over 60 years of age. The age-specific rate for the chronic sick over 65 years of age in the Birmingham hospitals at the time of the inquiry was 12 per 1,000 of the population in this age-group. Of those admitted in one year to one of these hospitals 79% died or were discharged within 4 months, so that in a hospital for the chronic sick there was quite an amount of acute illness. It was found that the marital status of patients had a considerable bearing upon their admission to, or retention in, the hospital. More than two-thirds of the patients were admitted from their own homes or from those of relatives and only one-half of the patients were willing to leave hospital if circumstances permitted.

F. A. E. Crew

438. **The Care of the Chronic Sick. IV. A Comparison of Data from Hospitals in the Stoke-on-Trent Area with Data from Western Road Infirmary, Birmingham**

C. R. LOWE and T. MCKEOWN. *British Journal of Social Medicine* [*Brit. J. soc. Med.*] **4**, 137–142, July, 1950. 3 refs.

439. **The Sex Ratio of Human Births Related to Maternal Age**

C. R. LOWE and T. MCKEOWN. *British Journal of Social Medicine* [*Brit. J. soc. Med.*] **4**, 75–85, April, 1950. 5 figs., 6 refs.

It is a common observation that in multiparae reproductive wastage is greater than in primiparae, and that the maternal organism is generally in better physiological condition before the first birth than after a series of pregnancies, especially if the pregnancies occur at short intervals.

The authors examined the sex ratio of total births, live births, and stillbirths at different maternal ages, using the figures provided in the Annual Reports of the Registrar-General for England and Wales and for Scotland. They found that the sex ratios of total births and live births decrease with maternal age, whilst those of stillbirths increase. They suggest that the increase in the sex ratio of stillbirths with maternal age accounts for the difference between live births and total births and that the decrease in the sex ratio of total births with maternal age is to be explained by changes in the sex ratio of abortions earlier than the twenty-eighth week.

F. A. E. Crew

440. **Poliomyelitis in Auckland, 1947–1949. An Epidemiological Study**

A. W. S. THOMPSON. *Journal of Hygiene* [*J. Hyg., Camb.*] **48**, 96–120, March, 1950. 12 figs., 2 refs.

This paper is a sequel to a similar report in 1948 and deals with nearly 350 cases of poliomyelitis which occurred in a population of about 350,000 in Auckland, New Zealand, during the period of high prevalence from October, 1947, to April, 1949.

The incidence per 10,000 reached 8·0 in the city, 15·4 in the country districts, and 21·5 in surrounding urban areas lying between the city and country. In general the incidence as measured by notifications was inversely related to population density. The author attributes abnormally high incidence in these urban areas to influx of rural dwellers in recent years, whereby the balance of immunity was disturbed. Unusually low incidence in one city area may have been related to the periodic effect of race meetings in increasing the local density. Families of cases showed no significant difference in composition from the average in the area. No correlation, either inverse or direct, was found between sanitary conditions in schools and the incidence of poliomyelitis. An interesting feature was the comparative rarity of cases in the neighbourhood of sewage-polluted bathing beaches.

[The paper provides a wealth of graphs and figures which will interest the armchair epidemiologist. Unfortunately, the statistics are so given as to throw a great deal of doubt on their validity; thus in the four contiguous urban areas with high attack rates, lying between the city and the country, the proportion of non-paralytic to paralytic cases is 2 to 1, although in the most densely populated area, said to have had the lowest attack

rate, no non-paralytic cases whatever were included. The abstracter suspects that in the newer residential districts around Auckland the quality of medical care leads to the diagnosis of non-paralytic poliomyelitis much more frequently than in the older, more densely populated, city. If this be so, considerable doubt is cast upon many of the arguments in this paper.]

W. H. Bradley

441. **Q Fever in California. II. Recovery of *Coxiella burneti* from Naturally-infected Air-borne Dust**

P. D. DeLay, E. H. Lennette, and K. B. DeOme. *Journal of Immunology* [*J. Immunol.*] **65**, 211–220, Aug., 1950. 1 fig., 32 refs.

A method is described by which infecting organisms present in particles in air can be trapped by sucking the air through a glass chamber in which beef-extract broth is nebulized. At the end of the run the residual beef-extract broth is collected and frozen solid. At convenient times it is thawed, centrifuged at 500 revolutions per minute for 5 minutes, and treated with penicillin to give a final concentration of 500 units per ml. After incubation at 4° C. for 4 to 5 hours, the material is injected into guinea-pigs either intraperitoneally, or intraperitoneally and subcutaneously. Any guinea-pig whose temperature rises to 104° F. (40° C.) or which shows signs of illness is killed and its blood or splenic tissue is inoculated into fertile hens' eggs. All remaining test animals are kept for 6 weeks and their blood is tested at the end of that time for complement-fixing antibodies to *Coxiella burnetii* (*Rickettsia burnetii*).

By this means (either by direct proof of infection of guinea-pigs or by demonstration of complement-fixing antibody in test animals) the authors have shown the presence of *C. burnetii* in dust-laden air from a dairy in Southern California and a sheep ranch in Northern California, and claim that air-borne rickettsial infection may occur in man in such places. *C. L. Oakley*

442. **The Importance of Air-borne Infection in the Epidemiology of Tuberculosis.** (Znaczenie zakaźenia wdechowego w epidemiologii gruźlicy)

J. Kwapoński. *Gruźlica* [*Gruzlica*] **18**, 118–140, Jan.–March, 1950. Bibliography.

The author reviews available experimental and epidemiological data, describes his own experience, and concludes that the factor of most importance in the epidemiology of tuberculosis is air-borne infection, and especially droplet infection. This occurs by close contact with human and animal cases of pulmonary tuberculosis. Dust infection is of secondary importance, because all the conditions required are seldom realized. The danger of air-borne tuberculous infection is greater when contact is closer and more frequent, and the infection more massive. In his view careful analysis of cases will reveal in 100% of them a history of exposure to a source of infection.

Preventive measures should include the isolation of tuberculous patients, with simultaneous detection of the particular source of droplet infection.

J. W. Czekalowski

443. **Incongruity between Clinical and *X*-ray Pictures of Silicosis.** (Rozbieznosci w obrazie radiologicznym i klinicznym krzemicy płuc)

W. Zahorski. *Medycyna Pracy* [*Med. Pracy*] **1**, 25–30, 1950. 12 refs.

Among 21,049 workers exposed to risk, the author found 1,000 suffering from silicosis. In about two-fifths of these a marked incongruity was noticed between the radiological picture and the clinical manifestations.

In 11·3% (of the total number of cases) the functional capacity of the lungs was more impaired than would have been anticipated from the radiological findings, whereas in 28·3% the clinical symptoms were comparatively mild in relation to the radiological picture.

It is believed that these incongruities depend to a certain extent on a constitutional predisposition of particular individuals to pulmonary emphysema, and that the individual biological properties of the pulmonary tissue constitute an important factor. Respiratory failure depends upon the extent of the emphysematous changes produced by the silicotic nodules.

The author suggests a new classification of pulmonary silicosis based on the clinical condition as well as on the radiological picture. *J. W. Czekalowski*

444. **Effect of Aluminium on the Silicosis-producing Action of Inhaled Quartz**

E. J. King, B. M. Wright, S. C. Ray, and C. V. Harrison. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **7**, 27–36, Jan., 1950. 14 figs., 19 refs.

After many unsuccessful attempts the authors have succeeded in preventing or retarding the production of silicosis in rats dusted daily with a mixture of aluminium and quartz, using a new cabinet and a new method of producing dust clouds (described by Wright in 1948). Rats were exposed for 18 hours a day to an atmosphere containing about 30,000 particles pure quartz per c.cm., on the one hand, and of quartz combined with 2% of powdered aluminium on the other. Previous experiments had been directed unsuccessfully to demonstrating that aluminium can exert its preventive or retarding action only if it is constantly renewed. An assessment was made of the fibrosis in sections of the lungs. The lesions induced by this technique differed from those induced by the single intratracheal injection technique. Silver-impregnated coronal sections of lung were examined for evidence of reticulin formation, and any circumscribed collection of reticulin fibrils in the lung parenchyma was designated as a " nodule ".

Nodular reticulosis was present in the lungs of quartz-dusted rats from about the 200th day, and fully developed collagenous silicosis from about the 300th day. The rats exposed to quartz and aluminium had almost no reticulosis in their lungs at 200 days, and only very slight reticulosis at 300 days. The rats in this group which survived the longest (about 400 days) had reticulin nodules only a little more advanced than those exposed to quartz alone at 200 days. There was just as much quartz in the lungs of the animals exposed to quartz and aluminium as in those of rats exposed to pure quartz. " A retardation of about 200 days, or possibly a preven-

tion, of the development of silicotic lesions in the lungs of animals has been secured by the inclusion of 2% of metallic aluminium powder in the quartz ".

[The most interesting problem raised by these experiments is whether experimental silicosis in animals was prevented or merely retarded. The bearing of this and similar investigations on the problem of human silicosis is yet unknown and, while results of experiments in human silicosis will be awaited with interest, it is useful to explore how fully aluminium can be relied upon as a preventive in animals. Meanwhile, suppression of industrial dust seems to be the only way in which there can be any confident control of this most serious of industrial diseases.] *A. J. Amor*

445. **The Effect of Granite on the Lungs of Rats**
E. J. KING, S. C. RAY, C. V. HARRISON, and G. NAGELSCHMIDT. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **7**, 37–41, Jan., 1950. 4 figs., 18 refs.

Animal experiments were used for the first time to supplement medical and environmental surveys of the influence of granite dust upon the lungs. For the experiments, fine granite dust collected from the actual working shed of a Cornish quarry was used. The washed and prepared dust, containing particles with a size range of from 1 to 5μ, was injected intratracheally into rats. The lungs were examined microscopically after 28, 100, and 250 days. Between 100 and 250 days the loose dust collections underwent no significant change and did not become collagenous. The hilar lymph nodes showed similar changes. In contrast to lesions induced by pure silica the granite lesions are smaller and less dense, and contain only a loose tangle of reticulin fibrils. Granite produces only a mild reticulin reaction, not comparable with the silicosis produced by quartz.
A. J. Amor

446. **Skin Cancer in the Engineering Industry from the Use of Mineral Oil**
C. N. D. CRUICKSHANK and J. R. SQUIRE. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **7**, 1–11, Jan.. 1950. 3 figs., 15 refs.

The authors describe: (*a*) a field trial involving the examination of the skin of the hands and forearms of 138 workers exposed to cutting oils in the " bar-automatic " machine shops of three factories in Birmingham; (*b*) an analysis of cases of scrotal cancer treated over a 10-year period at the United Birmingham Hospitals, which serve the largest light-engineering centre in England; (*c*) animal experiments which resulted in the production of benign tumours in rabbits painted with a specimen of used cutting oil from the machine sumps. Of the workers 80% had oil folliculitis, clothing and skin (including thighs and genitals) showing oil contamination. Workers exposed for longer periods had hyperkeratoses, 60% of those exposed for more than 15 years being affected. The hyperkeratoses were of two types, flat, white, circular, smooth plaques 1 to 2 mm. across, and raised, rugose, pigmented warts, round, oval, or irregular. Both were similar to those present in tar workers and mule spinners. None of the men examined had previously worked with tar or pitch. Some had in previous occupations worked with oil or suds which may account for hyperkeratoses noted in men with less than 5 years' exposure. Statistical testing showed that almost certainly the hyperkeratoses could be attributed to occupational exposure. One case of scrotal cancer was found.

The hospital analysis revealed that, of 34 cases of scrotal cancer traced, 13 were in pitch or tar workers, 9 were in a doubtful category, and the remaining 12 patients had been exposed to oil (6 machine-tool operators exposed to cutting oils, 5 in engineering jobs, and 1 in the cotton and engineering industries). The average age of oil workers was significantly lower than that of the pitch workers. Approximately one-third of the patients in the hospital series died within 2 years. That 6 of the 34 patients with scrotal cancer followed occupations similar to those of the workers in the field trial indicates that the occurrence of scrotal cancer in this group was not an isolated event. Since the workers had oil folliculitis, implying contamination with oil, it may be expected that if the oil is carcinogenic other cases will follow. Some cutting oils used were shown to be capable of producing hyperkeratoses, which are to be regarded as signs of a cancer risk. The oils in use have varied considerably during the past 15 years, and automatic tools have been in use on a large scale only within the past 20 years. Although oils in use may be carcinogenic, it is too early for their effect to have become manifest. A plea is made for better protection and medical inspection, and for investigation of the biological properties of various fractions and also of the possibility of producing non-carcinogenic oils suitable for use in the engineering industry. *A. J. Amor*

447. **Asbestosis in Asbestos Textile Plants.** (Pylica azbęstowa w przędzalni i tkalni azbestu)
E. PALUCH, J. KUBACKI, L. MIKULSKI, K. MROZOWSKI, and F. SEKURACKI. *Medycyna Pracy* [*Med. Pracy*] **1**, 2–24, 1950. 5 figs., 17 refs.

The authors report on the dust conditions in the air, and on the medical examination of the employees, in two asbestos factories. The dust content was estimated by means of a micro-impinger, and was shown to be between 2 and 24 times greater than the standard of 5 million particles per cubic foot (M.P.P.C.F.) recognized by the Industrial Health Conference at Boston in 1948. The geometric mean of dust particles as estimated by the thermo-precipitator slide method of Green and Watson ranged from 0·62 to 0·76 μ. The highest concentration of dust (over 50 M.P.P.C.F.) was found in the preparatory department; there was a very high concentration (25 to 50 M.P.P.C.F.) in the carding, spinning, and weaving departments and a moderate one (5 to 25 M.P.P.C.F.) in the finished-goods department.

The authors discuss 10 cases of asbestosis (6 in men) among the employees of different departments in asbestos plants. One case was a very early one, 4 cases were in stage I, 4 cases in stage II, and one in II–III. There was in these cases an accurate correlation between the dust exposure (measured in thousand million particle-years) and the stage of asbestosis.

Technical, medical, and prophylactic problems are discussed. *J. W. Czekalowski*

Anatomy and Cytology

448. **The Nerve Supply of the Kidneys.** [In English] G. A. C. MITCHELL. *Acta Anatomica* [*Acta anat., Basel*] **10**, 1–37, 1950. 8 figs., bibliography.

The origin, arrangement, and connexions of the renal nerves have been investigated by the author at the University of Manchester in 23 human subjects (20 full-term infants and 3 adults). The infant dissections were performed, under a watery solution containing about 25% of alcohol, with the help of a low-power dissecting microscope, and the procedure was facilitated by injecting some of the solution into the areolar tissue around nerves and plexuses. The presence of nerve fibres or cells was always confirmed microscopically if any doubt existed. Any new or unusual arrangement noted was invariably confirmed by one or more independent skilled observers before the material was removed for sectioning.

As a result of these investigations the author concludes that the nerve supply of the kidney comes from the following sources: (1) The coeliac plexus, the renal branches of which are constant, unequal in size, variable in number (4 to 8), and asymmetrical. They arise from the homolateral coeliac (semilunar) ganglion and its aortico-renal subdivision, or from nerve bundles connecting the two ganglia, and they include contributions from the vagus and phrenic nerves. (2) The thoracic splanchnic nerves. The author was not able to confirm the presence of the " ramus splanchnicus supremus " described by Wrisberg as sometimes supplying the kidney. The greater and lesser splanchnic nerves contribute to the nerve supply of the kidney by way of their branches to the coeliac and aortico-renal ganglia. Some of their branches also pass directly to the renal plexus. The least splanchnic nerve (which was usually present in this series of dissections) commonly joins the renal plexus directly. (3) The lumbar splanchnic nerves. Branches from the 1st and 2nd lumbar ganglia pass directly to the posterior part of the renal plexus or may end in a posterior renal ganglion. (4) The upper parts of the intermesenteric nerves. Renal branches arise from the outermost intermesenteric nerves approximately at the level of the commencement of the superior mesenteric plexus and pass directly to the renal plexus. (5) The lower parts of the intermesenteric nerves. Renal branches arise opposite the origin of the inferior mesenteric plexus and/or from the superior hypogastric plexus and, passing upwards, join the lower and outer part of the renal plexus. Except at their termination they remain quite separate from other renal nerves. They invariably communicate with the superior spermatic nerves and also supply filaments to the lower part of the renal pelvis and upper end of the ureter. It is suggested that when there is a caudal shift in the blood supply of the kidney, there is a corresponding caudal shift in the nerve supply, so that recurrent nerves arising from the superior hypogastric plexus run upwards across the posterior abdominal wall to join the renal plexus. Probably the parasympathetic supply to the ureters, renal pelvis, and renal collecting tubules is drawn from the pelvic splanchnic nerves, and the fibres pass to their destination by way of the inferior hypogastric plexus, hypogastric nerves, superior hypogastric plexus, intermesenteric nerves, and the branches described above.

The kidneys receive a more abundant nerve supply in proportion to their size than any other abdominal viscus except the suprarenal glands. The majority, but by no means all, of the nerves lie near the main renal artery; some approach this vessel only in the hilum of the kidney, while others lie in contact not with the main vessel, but with its branches. If accessory arteries are present the plexus may be divided. The roots of the plexus, drawn from the corresponding semilunar, aortico-renal, and inferior mesenteric ganglia, run obliquely outwards, at first above the renal artery. Approaching the organ they coalesce into 2 to 4 thicker filaments which embrace the artery and are interconnected by fine filaments. No large filaments lie anterior to the renal vein or posterior to the pelvis, but fine filaments supplying vein, pelvis, and renal capsule lie in these positions. The renal ganglia are never absent, but may be microscopic in size and variable in number and position. The aortico-renal ganglion represents a detached lower and outer part of the coeliac ganglion. It may be replaced by several small ganglia or, occasionally, be fused with the coeliac ganglion. It lies above, or anterior to, the renal artery near its origin. It is connected with the coeliac and superior mesenteric ganglia and supplies a variable number of filaments to the renal plexus. Other ganglia of varying size may be seen on any of the renal nerves, most commonly at points of branching or union. They tend to become progressively smaller as the kidney is approached, and are more numerous in infancy. The largest and most constant is the posterior renal ganglion which lies postero-superior to the renal artery. An anterior renal ganglion is sometimes found close to the origin of this vessel. The fibres in the nerves of the renal plexus must be partly pre- and partly post-ganglionic since some of them will relay not in the coeliac or aortico-renal ganglia, but in these small ganglia. Microscopically, both medullated and non-medullated fibres can be distinguished in the plexus.

The paper also includes a valuable historical review of the growth of knowledge of the renal nerve supply.

H. Hughes

449. **Investigations into the Morphogenesis of the Villi of the Human Ovum Grown *in vitro*.** (Badania nad morfogenezą kosmków jaja ludzkiego hodowanych *in vitro*) E. HOWORKA. *Polski Tygodnik Lekarski* [*Polsk. Tyg. lek.*] **5**, 921–922, June 12, 1950. 1 ref.

Parts of human placental villi were grown in a hanging drop of plasma or plasma diluted with Tyrode solution for 2 to 10 days. The environment was changed every

1 to 3 days. Afterwards the tissue culture was fixed and examined histologically. The following phenomena were observed. (1) Coagulation of plasma. The plasma passed through different stages of intensity of coagulum-formation up to formation of a well-defined reticulum. (2) Liquefaction of coagulating plasma around the explanted villi. The time of fibrinolysis corresponded to that of coagulation. (3) Changes on the surface of the explanted villi took place at this time, and stopped when coagulation and fibrinolysis were completed. (4) Increase in the elements of the trophoblast. The change of small cells into large required the presence of a dense reticulum in the medium, whereas the appearance of polynuclear elements coincided with that of fibrinolytic properties. *J. W. Czekalowski*

450. **Cytological Phenomena associated with Experimental Alterations of Secretory Activity in the Adrenal Cortex of Mice**
R. A. MILLER. *American Journal of Anatomy* [*Amer. J. Anat.*] **86**, 405–438, May, 1950. 18 figs., 33 refs.

The cytological changes in the glomerular and fascicular zones of the adrenal cortex of mice in experimentally induced atrophy and hypertrophy are similar. By experimental methods either zone can be stimulated or depressed independently of the other. Since the number of mitochondria and the concentration of lipid droplets are inversely correlated in atrophy and hypertrophy, it is suggested that mitochondria are intimately involved in the formation of lipid and disappear as visible entities in the course of this process. The various experimentally induced modifications of the cells of both the glomerular and fascicular zones are consistent with the theory that stimuli to secretory activity cause a proliferation of mitochondria and discharge of lipid. *R. J. Ludford*

451. **The Innervation of the Coronary Vessels.** (Inervacion de los vasos coronarios)
K. T. TCHENG. *Archivos del Instituto de Cardiología de Mexico* [*Arch. Inst. cardiol. Mex.*] **20**, 297–313, June 30, 1950. 9 figs., 27 refs.

452. **Researches on the Morphology and Classification of the Oligodendroglia.** (Ricerche sulla morfologia e classificazione della oligodendroglia)
M. P. D'AGATA. *Rivista di Neurologia* [*Riv. Neurol.*] **20**, 81–127, March–April, 1950. 32 figs., bibliography.

The author has carried out a histological examination of human and animal brains, with special study of the glial cells. While he admits that neuroglia, microglia, and oligodendroglia (with Hortega's 4 types) can be more or less clearly distinguished, he finds that there are many transitional cell forms which do not easily fit into a definite category. He is therefore inclined to believe that only one single glial element exists, the morphology of which varies with the age, function, and site of the cell.

Hortega's classification, being based on microscopical appearances only, is therefore, in the author's opinion, insufficient. However, as he is unable to offer a classification based on functional criteria, he suggests that for the time being Hortega's earlier classification should be used, which distinguishes between interfascicular glia, perineuronal satellite glia, and vascular satellite glia.
F. K. Kessel

453. **Some Data Concerning the Growth and Development of the Cerebral Cortex in Man. II. Postnatal Growth Changes in the Cortical Surface Area**
O. A. TURNER. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **64**, 378–384, Sept. 1950. 1 fig., 12 refs.

This paper is the second in a series of studies of the growth of the cortex, of which the first (*Arch. Neurol. Psychiat., Chicago*, 1948, **59**, 1) was concerned with the alteration of the fissural pattern of the developing brain, the present paper dealing with the changes in the free (visible) cortical surface area. Fourteen brains, from persons whose age ranged from 3 weeks to 24 years, were studied. The method of determining the surface area was that used by Wagner (1862), the gyri being covered with gold leaf and the area then being calculated by dividing the weight of gold used by the specific gravity and the thickness of the leaf. Surface-area measurements were made of the cerebrum as a whole, of each hemisphere separately, and of the frontal, parietal, temporal, and occipital lobes of both sides taken together.

When the free surface area of the two hemispheres, taken together or separately, is plotted against age, a definite growth pattern can be recognized, general growth occurring between birth and the sixth year, with a very early and rapid threefold increase of area between birth and 2 years followed by a less striking increase (about 25%) between 2 and 6 years. Beyond the sixth year there appears to be little change in the total free surface area. No evidence was found of any difference in surface area between the two hemispheres [although the author's graph shows a relatively greater increase of the left hemisphere at the age of 10 years]. These two phases of rapid growth are also manifest in all the lobes except the occipital, in which there is a steady three- to fourfold increase from birth to 6 years. In the frontal lobe alone is there indication of further development up to the tenth year, by which time the surface area has increased fourfold since birth. The temporal lobe increases threefold. Of the various lobes, the parietal appears to undergo a greater expansion at a greater rate than any other—about fivefold.

A short review of earlier work on the estimation of cortical surface areas is included. *J. B. Stanton*

454. **The Innervation of Human Skin. I. The Cerebrospinal Component in Innervation of the Skin.** (Studi sull'innervazione del pelo umano. I. La componente cerebro-spinale dell'innervazione del pelo)
F. ORMEA. *Dermosifilografo* [*Dermosifilografo*] **25**, 235–249, May, 1950. 8 figs., 1 ref.

455. **The Innervation of Human Skin. II. The Vegetative Component in Innervation of the Skin.** (Studi sull'innervazione del pelo umano. II. La componente vegetativa dell'innervazione del pelo)
F. ORMEA. *Dermosifilografo* [*Dermosifilografo*] **25**, 250–260, May, 1950. 7 figs., bibliography.

Physiology and Biochemistry

456. **The Composition of the Surface Skin Fat (" Sebum ") from the Human Forearm**
R. M. B. MACKENNA, V. R. WHEATLEY, and A. WORMALL. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **15**, 33–47, July, 1950. 1 fig., 37 refs.

Surface skin fat (" sebum ") was collected from groups of normal males by immersing both forearms successively in 2 litres of acetone for 3 minutes. The acetone was then evaporated and the residue purified by dissolving it in chloroform, filtering, and evaporating to dryness. The sebum thus obtained was weighed and each batch was analysed. The two forearms were found to secrete sebum at the rate of 10 to 25 mg. an hour during a period of 3 to 6 hours between successive extractions. Mixed sebum from 107 subjects contained 29% free fatty acids, 36% combined fatty acids, and 32% unsaponifiable matter. Chromatographic analysis of the unsaponifiable fraction yielded hydrocarbons (46%), cholesterol (14%), saturated and unsaturated alcohols (8%), and some unidentified compounds. The presence of about 5% squalene in sebum was established. A very small amount of nitrogenous material was present, chiefly as lipid and urea. Sebum contained vitamin E, but no significant amount of any other fat-soluble vitamin or of β-carotene or ergosterol was found. *James Marshall*

457. **Physiology of Skiing.** [In English]
E. H. CHRISTENSEN and P. HÖGBERG. *Arbeitsphysiologie* [*Arbeitsphysiologie*] **14**, 292–303, 1950. 6 figs., 3 refs.

Experiments were performed by skiers carrying a Douglas bag in a special rucksack. Some of them travelled on the level and others uphill. Determination of metabolic rate began when metabolism had apparently reached a steady state, usually 5 minutes or so after starting. The persons on whom the tests were made were in good training, and in one oxygen consumption reached 5·2 litres a minute, which is close to the highest value recorded in the literature in a runner.

The oxygen intake increased linearly with increasing speed, but it is doubted whether energy output increased similarly, though the oxygen debt was never determined. The climatic conditions were almost uniform, since all experiments were finished within a few hours. In 2 women in good training the oxygen intake was 4·17 litres a minute and 64·5 ml. per minute per kg. body weight respectively, possibly the highest values seen in women.

Although skiing consumes much energy it was found to be more economical in physical effort than walking on the snow, a fact of importance in civil and military movement during winter.

Albuminuria was seen in nearly all the participants, but was less marked as they got into better training. Erythrocytes were found in the urine in one-quarter of persons tested.

Some skiers transport loads on light sleighs, which they drag behind them, and experiments were performed in which 30 kg. was first carried on a sleigh, which weighed 8 kg., and then put in a rucksack. Though the energy output was 15% less when the rucksack was used, most performers found it more agreeable to drag the sleigh, which took weight off their shoulders. In some persons, notably adolescents, pulse rate rose to 250 or more.

It is evident that skiing, which makes great demands on the body, is an excellent exercise for acquiring general physical fitness in a short time. Older people should take care not to overstrain themselves when using skis. Results obtained must of course vary with the degree of skill of the performers. *G. C. Pether*

458. **The Role of Ascorbic Acid in Corneal Vascularization**
F. W. CAMPBELL and I. D. FERGUSON. *British Journal of Ophthalmology* [*Brit. J. Ophthal.*] **34**, 329–334, June, 1940. 13 refs.

Standard heat injuries were inflicted on the cornea of scorbutic and control guinea-pigs. The incidence of vascularization in the course of healing was significantly higher in the scorbutic than in the normal animals, and its presence was not significantly related to the time taken for epithelial healing in either group. It is suggested that corneal injury may unmask a deficiency of ascorbic acid in the cornea which does not otherwise become manifest, and that vascularization represents an attempt to meet the extra metabolic needs of new formation of collagen. It is further, though tentatively, suggested that metabolites, accumulated as a result of inability to meet such metabolic needs, may provide the humoral stimulus to vascularization already postulated by Campbell and Michaelson. *Katharine Tansley*

459. **Acute Experimental Parathyroid Insufficiency. I. Plasma Levels of Calcium and Inorganic Phosphorus in Various Forms of this Insufficiency.** (Estudios acerca de la insuficiencia paratiroidea experimental aguda. I. Valores del calcio y del fósforo inorgánico del plasma sanguíneo en las diversas formas de esta insuficiencia)
J. M. DE CORRAL and J. M. ALVARO-GARCÍA. *Revista Española de Fisiología* [*Rev. esp. Fisiol.*] **6**, 53–85, June, 1950. 4 figs., 31 refs.

In experiments carried out at the Cajal Institute, Madrid, the mean plasma content of calcium in 36 dogs was found to be 10·5 mg. per 100 ml. (S.D. 1·5), and that of inorganic phosphate in 32 dogs 4·2 mg. of phosphorus per 100 ml. (S.D. 1·0). The Ca/P ratio was roughly equal to that in hydroxyapatite.

Total parathyroidectomy was carried out on 33 dogs with the following results: (1) Convulsive tetany developed in 16, starting with hypotonia and ataxia, followed

by a hypertonic stage, and ending in convulsions on the third day or later. Of these 16 dogs, 3 which were treated with calcium gluconate and vitamin D survived. The others died within 11 days, the plasma calcium level falling to half, and the phosphate level rising to double, the pre-operative value. There was no constant relationship between changes in plasma calcium or phosphate levels or the Ca/P ratio and the onset of convulsions or death. (2) A further 12 dogs developed tetany without convulsions. Of these, 4 developed hypertonia, 3 dying in a few days, possibly in the pre-convulsive stage, while the fourth, which might have had an incomplete parathyroidectomy, recovered spontaneously; in this group only small changes in serum calcium and phosphate levels were found. In 3 others, in which severe dyspnoea occurred, the calcium and phosphate changes were as marked as in the convulsive group; 2 of these dogs died and the third was killed. Another 2 dogs developed diarrhoea and vomiting, one dying with intestinal haemorrhage and marked changes in plasma calcium and phosphate levels, and the other recovering spontaneously. Asthenia was the only change in the 3 other dogs, all of which died. In these, too, the changes in calcium and phosphate levels were marked. (3) The remaining 5 dogs developed no symptoms of tetany; a small fall occurred in the plasma calcium level, but no change in the phosphate level. Parathyroidectomy was shown to be incomplete in 2 of them. The other 3 died in a few days and might have been in the pre-convulsive stage.

In all the animals, the plasma phosphate level was more inconstant and varied over a much wider range than that of calcium. The authors believe that the essential result of parathyroidectomy is a fall in the plasma calcium content, the phosphate level rising as a consequence of this fall. The high plasma level of phosphate in tetany may be due to poor renal excretion together with an increase in circulating phosphate caused by the tetanic muscular contractions. *M. Lubran*

460. **Mechanism of Muscular Fatigue in Adrenalectomized Animals**

E. RAMEY, M. S. GOLDSTEIN, and R. LEVINE. *American Journal of Physiology* [*Amer. J. Physiol.*] **162**, 10–16, July, 1950. 5 figs., 14 refs.

The authors describe experiments on the production of muscular fatigue in adrenalectomized and normal rats, and in muscle preparations made from them.

The rats were forced to swim in water at 35° C. Normal rats swam for periods of up to 3 hours and showed no ill effects. The adrenalectomized animals showed signs of fatigue after 10 to 20 minutes and sank to the bottom of the tank, completely exhausted, after 30 minutes. Breathing had ceased but the heart was still beating. The lungs contained air. There was no significant difference between the glycogen content of the muscles of the two groups after exercise.

In vitro, experiments were performed on preparations of phrenic nerve and hemidiaphragm and on strips of oblique abdominal muscle immersed in Ringer solution. The preparations were stimulated by brief faradic impulses at 6 per minute and the contractions were recorded on a kymograph. Recordings show that there was no difference in the rate of development of fatigue in muscle from adrenalectomized and from normal rats stimulated for periods of up to 5 hours. This was true of preparations stimulated directly and through the motor nerve.

Because there is no difference in the contractility of muscle between adrenalectomized and normal rats, the rapid onset of fatigue in the former must be due to failure of the necessary supply of nutrients to the working muscle, this supply being achieved in the normal animal by a great increase in blood flow. *R. P. Foggie*

461. **Psychic Stimulation of Prostatic Secretion**

L. C. CLARK and P. TREICHLER. *Psychosomatic Medicine* [*Psychosom. Med.*] **12**, 261–263, July–Aug., 1950. 1 fig., 11 refs.

The secretory activity of the prostate, in this experiment, was assessed by the rate at which acid phosphatase was excreted. Urine samples collected before, during, and after the stimulus were tested with phenolphthalein phosphate (Huggins). The sexual stimulus consisted of the showing of two or more short pornographic films. In 4 out of 5 male subjects exposed to this stimulus there was an increase in the rate of production of acid phosphatase. The fifth subject was embarrassed, almost repelled, by the films; this may explain the absence of increase in his case. None of the subjects experienced an erection, but all reported that they were sexually aroused; erection might have occurred if each had seen the film alone and not in a group. In two subjects the excitement associated with performing in a play produced changes in prostatic activity comparable to those which followed the sexual stimulus. *Desmond O'Neill*

462. **Electromyographic Studies of M. Biceps Brachii during Normal Voluntary Movement at the Elbow**

W. E. SULLIVAN, O. A. MORTENSEN, M. MILES, and L. S. GREENE. *Anatomical Record* [*Anat. Rec.*] **107**, 243–251, July, 1950. 2 figs., 6 refs.

The authors, working at the University of Wisconsin, set out to determine whether, during a given voluntary movement in a normal human subject, a particular muscle was active, and whether its activity varied during that movement. Electromyography was used as the method of investigation and the activity of the biceps brachii muscle analysed during movements of the elbow, recordings being made from 8 normal subjects. The electromyograph used consisted of an electrocardiograph adapted for the purpose by the inclusion in the subject-circuit of an amplifier which increased the sensitivity ten-fold. Records were made on standard electrocardiographic film moving either at 2·5 or 5·0 cm. per second. Interference was reduced by working in a screened room and by interposing a screen between the electromyograph and the operator. Surface electrodes of zinc, 1 cm. in diameter, were used, held in place by liquid adhesive, and standard positions for the electrodes on the parts of the muscle continuous with the long and short heads of origin were employed throughout. Records were taken during flexion (acceleration at

the elbow) and extension (negative acceleration at the elbow) and with the arm held (zero acceleration at the elbow) in positions of 135, 90, and 45 degrees of flexion, with no load and with loads of 1 and 2 kg. Repeated records were taken from the same subject at irregular intervals over a period of 10 months

Repeated recordings from the same subject were usually similar in pattern, but those taken under identical conditions from two or more subjects might differ in pattern and in amplitude. Deflections were shown which began at or near initiation of flexion, increasing in amplitude during the first third or half of the record and then maintaining an irregular plateau to the end of movement. During extension the pattern was considerably more variable, while with the arm held there was continuous activity, with a relatively uniform record. An analysis of the patterns of potentials recorded under the various conditions is given.

[The technique and apparatus used did not permit of any quantitative measurement or analysis of potentials—they are therefore of use only in the analysis of movement, and have little clinical application.] *Kenneth Tyler*

463. **Role of Somesthetic Stimuli in the Development of Sexual Excitation in Man. A Preliminary Report**
M. HERMAN. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **64**, 42–56, July, 1950. 14 refs.

464. **Explosive Decompression at High Altitude**
S. GELFAN, L. F. NIMS, and R. B. LIVINGSTON. *American Journal of Physiology* [*Amer. J. Physiol.*] **162**, 37–53, July, 1950. 11 figs., 25 refs.

The authors studied the effects on rats, placed in a compression cylinder, of explosive decompression to pressures equivalent to that at 75,000 ft. (22,500 m.), and the effects of subsequent rapid recompression or recompression at a rate simulating that obtaining in free fall. The survival time after sudden decompression becomes progressively shorter up to an altitude of 52,000 ft. (15,600 m.), after which it remains constant at about 30 seconds in air and 40 seconds in oxygen. At this level (pressure of 77 mg. Hg), even in an atmosphere of 100% oxygen, the oxygen pressure would not be significantly greater than the combined alveolar vapour and carbon-dioxide pressures. Below this critical level the difference between the survival times in oxygen and air widens sharply. Pre-oxygenation increases the survival time. Rapid decompression *per se*, even up to 75,000 ft., is not fatal to rats. Unless recompressed quickly, however, they die from anoxic anoxia. The main pathological change is complete haemorrhagic consolidation of the lungs.

The survival rates of rats recompressed at a free-fall rate from various altitudes in both air and oxygen are given. In air 25% survive from 60,000 ft. (18,000 m.) and 100% from 50,000 ft. (15,000 m.); in oxygen 50% survive from 75,000 ft. and 100% from 60,000 ft. The better chances of survival in oxygen are due to pre-oxygenation and the fact that the increase in pressure during recompression becomes quickly significant below 52,000 ft. in oxygen. *R. P. Foggie*

CIRCULATORY SYSTEM

465 (*a*). **A Quantitative Study of the Response to Cold of the Circulation through the Fingers of Normal Subjects**
A. D. M. GREENFIELD and J. T. SHEPHERD. *Clinical Science* [*Clin. Sci.*] **9**, 323–347, 1950. 13 figs., 22 refs.

Observations were made at Queen's University, Belfast, on the blood flow through the distal 2·8 cm. of the index finger as measured by plethysmographic and calorimetric methods. (The special calorimeter used is illustrated.) The plethysmographic method is misleading when the finger is cooled, owing to constriction of the capacity vessels in the digit. However, these vessels relax when the temperature rises above 32° C. and the method is then valid.

The heat loss of the index finger, as measured in the calorimeter, was used as an index of blood flow in 23 observations carried out on 14 subjects. With the water bath at between 0° C. and 6° C. almost complete cessation of blood flow was produced for 5 to 10 minutes; there was then an increase in blood flow to between 30 and 98 ml. per 100 c.cm. of finger per minute. Similar but smaller changes were observed at temperatures between 6° and 12° C. At 12° to 15° C. there was no initial constriction and the flow was usually less than at either of the lower temperature ranges. At 0° to 6° C. pain was felt in the finger when the blood flow was sufficiently small, but no pain was felt during a large vasodilatation in response to cold. It is concluded that pain is felt when the temperature gradient between the outside and inside of the finger is small and the internal temperature low, but not when the gradient is steep and the internal temperature high.

[It is not possible to abstract this long paper satisfactorily. Those interested must consult the original.] *A. T. Macqueen*

465 (*b*). **The Average Internal Temperature of Fingers Immersed in Cold Water**
A. D. M. GREENFIELD, J. T. SHEPHERD, and R. F. WHELAN. *Clinical Science* [*Clin. Sci.*] **9**, 349–354, 1950. 5 figs., 2 refs.

In an investigation into the vascular reaction to local cold, carried out at Queen's University, Belfast, the following method was used for measuring the internal temperature of the finger. The distal 2·8 cm. of forefinger was immersed in a special calorimeter (see Abstract 465 (*a*)) and temperature was measured every minute. The circulation to the finger was then suddenly arrested by inflating a cuff surrounding its base; by measurement of the heat subsequently transferred to the calorimeter it is possible to determine the average temperature of the finger at the moment of arrest of the circulation. The instrument was calibrated by transferring fingers, with the circulation arrested, from baths at known temperatures to the calorimeter and measuring the heat released. Nineteen experiments were performed on 12 subjects. It was found that at the height of cold vasodilatation due to immersion in a stirred calorimeter at 0° to 4° C., the average internal temperature of the finger was 20° to 30° C. The temperature gradient in the

finger varied with the difference between its average internal temperature and that of the water in the calorimeter.

It is claimed that by this method the structure of the finger is not disturbed (as it is when a thermo-electric couple is inserted) and that the over-all average temperature is obtained instead of that of a very small, localized area. *A. T. Macqueen*

466. **Individual Differences in Vascular Responses and their Relationship to Cold Tolerance**
M. E. BADER and J. MEAD. *Journal of Applied Physiology* [*J. appl. Physiol.*] **2**, 608–618, May, 1950. 3 figs., 5 refs.

Records were taken of the digital volume, blood pressure, and respiratory rate of human subjects subjected to a variety of stimuli including immersion of the feet in ice-water for one minute. Chilling of the feet produced marked initial vasoconstriction in the fingers, as indicated by a reduction in digital and pulse volumes. In some subjects values then tended to return to, or rise above, the control figures, although the feet were still immersed; in others they remained low throughout the period of immersion. As an index of the degree of return, the ratio of the control pulse volume to the maximum volume in the later part of the immersion period was calculated and is called the sensitivity index (S.I.) A close correlation was found between the physical performance and the S.I. of individuals exposed to Arctic weather under bivouac conditions at Fort Churchill, Manitoba; in general, the S.I. was low in the more efficient individuals and high in the least efficient. In a further test, 6 subjects under natural conditions at a temperature of $-10°$ F. ($-28{\cdot}3°$ C.) were given a simple manual task (untying of knots). The individual with the highest S.I. was unable to continue after 8 to 14 minutes owing to pain in the hands, while the individual with the lowest S.I. continued for 40 to 60 minutes. However, it is stressed that although correlation between digital vascular response and cold tolerance was demonstrated for groups of individuals, there were notable individual exceptions and the cold immersion response cannot be regarded as a specific indication of his performance under cold stress.

In men studied after a 10-day Arctic bivouac less pain was experienced and there was a smaller rise in blood pressure during immersion of the feet in ice-water than before. Apart from this, none of the other physiological indices of response to cold studied showed any marked relation to cold tolerance under field conditions.
R. P. Foggie

467. **Use of Radioactive Phosphorus in Studies of Fetal Circulation**
N. B. EVERETT and R. J. JOHNSON. *American Journal of Physiology* [*Amer. J. Physiol.*] **162**, 147–152, July, 1950. 7 refs.

Physiological saline labelled with radioactive phosphorus was injected into the jugular and umbilical veins of foetal guinea-pigs and dogs near term; the radioactivity of blood samples drawn simultaneously from the right and left ventricles was measured about 18 minutes later. It was found that three-fourths of the umbilical-vein blood passes through the foramen ovale to the left side of the heart and one-fourth reaches the right side. Three-fourths of the blood from the anterior vena cava passes to the right ventricle and one-fourth to the left ventricle.

Injection of the umbilical vein and sampling of blood from the umbilical artery showed the circulation rate in both foetal guinea-pigs and foetal dogs to be about 18 seconds. *R. P. Foggie*

468. **The Nature of Plasma Antithrombin Activity**
P. D. KLEIN and W. H. SEEGERS. *Blood* [*Blood*] **5**, 742–752, Aug., 1950. 4 figs., 23 refs.

The fact that two separate effects on thrombin are taking place must be recognized in plasma antithrombin investigations. The first effect, concerned with disposal of the thrombin, can be determined by estimating the thrombin left after the antithrombin reaction has been completed; the second effect is associated with interference with the thrombin–fibrinogen reaction, and thrombin activity is not affected by it. In the former effect plasma antithrombin is uninfluenced by the presence of heparin. The quantity of thrombin destroyed is constant for any given amount of defibrinated plasma, being independent of the initial thrombin concentration provided the latter is greater than the antithrombin capacity of the plasma. In bovine plasma this antithrombin capacity is approximately 710 units of thrombin. If the initial quantity of thrombin is less than the antithrombin capacity of the plasma, a certain amount of thrombin may remain free after equilibrium has been reached.

Fibrin itself may diminish thrombin activity in a solution by adsorption; heparin increases this adsorption of thrombin on fibrin, but albumin decreases it. Lysis of the fibrin releases this adsorbed thrombin. Thus the general view that heparin has an antithrombic effect in association with a plasma co-factor can be explained on the basis that this mechanism interferes with the thrombin–fibrinogen reaction, which itself does not destroy thrombin. *John F. Wilkinson*

469. **The Prothrombin Conversion Accelerator of Serum (SPCA): its Partial Purification and its Properties compared with Serum AC-globulin**
B. ALEXANDER, R. GOLDSTEIN, and G. LANDWEHR. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 881–895, July, 1950. 5 figs., 31 refs.

A number of properties of purified SPCA (serum prothrombin conversion accelerator) and Ac-globulin are compared, and some further properties of SPCA are reported. Details of preparation of the various serum fractions used are given.

SPCA will accelerate prothrombin conversion in a one-stage system in which accessory plasma factors are provided (SPCA activity), but not in a two-stage system in which they are absent. Ac-globulin is active in such a two-stage system, and also contains the factors necessary for SPCA activity to occur. It follows that SPCA

activity may depend upon the presence of a non-prothrombin plasma factor. Accordingly, human serum two hours old (with no SPCA activity alone) was mixed with human prothrombin-free plasma; this mixture accelerated prothrombin conversion in a two-stage system more than did the plasma alone. Removal of SPCA from the aged serum by adsorption with barium sulphate brought the prothrombin-conversion velocity and yield of thrombin to a minimum. SPCA may therefore be active in a two-stage system (showing Ac-globulin activity) if non-prothrombin plasma factors are provided, and if Ac-globulin itself contains such a factor or factors. SPCA activity appears only after a period of 1 to 5 minutes has elapsed after addition of plasma factor(s), suggesting an interaction between the two.

Ac-globulin showed about one-eighth the SPCA activity of the purest SPCA fraction, and the observation of Ware and Seegers that serum Ac-globulin does not accelerate prothrombin conversion in a plasma diluent was confirmed. On the other hand, Ac-globulin was shown to be highly active on purified human or bovine prothrombin. In addition, it was found that beef serum rich in Ac-globulin would accelerate bovine prothrombin conversion in a bovine prothrombin-free plasma (that is, the effect is not due to addition of non-specific plasma factors in which human plasma is relatively deficient).

The adsorbability of SPCA and Ac-globulin on to $BaSO_4$ and $BaCO_3$ was compared; whereas the former may be completely removed by shaking with 25 mg. of $BaSO_4$ or 100 mg. of $BaCO_3$ per ml., not all Ac-globulin activity can be removed even with higher adsorbent concentrations. The remaining Ac-globulin activity is, however, apparent only on human prothrombin in a human diluent, and the authors are of the opinion that this may be due to the non-specific heterologous-species effect of a constituent of bovine plasma, which they discuss.

Comparison was also made of the effect of SPCA and serum Ac-globulin in accelerating prothrombin conversion in aged plasma. It is suggested that Ac-globulin contains at least two components, a labile and a stable factor, the latter possibly being SPCA. It was also shown that SPCA accelerated the clotting of normal and haemophilic blood (even in the case of a haemophilic subject who had become completely resistant to the effect of anti-haemophilic globulin in normal plasma), and of blood heparinized or collected in siliconized vessels. No proteolytic activity could be demonstrated, and in view of the data summarized above, the authors conclude that SPCA formation underlies the autocatalytic mechanism of prothrombin conversion. This hypothesis is fully discussed. *E. A. Brown*

470. **Attempts to Demonstrate a Specific Erythropoietic Hormone.** (Versuche zum Nachweis eines spezifischen erythropoietischen Hormons)
G. RUHENSTROTH-BAUER. *Archiv für Experimentelle Pathologie und Pharmakologie* [*Arch. exp. Path. Pharmak.*] **211**, 32–56, 1950. 3 figs., bibliography.

Contrary to the assertions of other investigators, the author states that, in his experience, injections of human serum into rats do not produce a significant rise in the erythrocyte count during the next 4 days. Rabbits, which are more suitable subjects for studies on erythropoiesis, were used in further investigations, but as serial erythrocyte counts were found to be unsatisfactory, reticulocyte counts, made directly in a counting chamber, were used in assessing the degree of erythropoiesis following venesection (normally 15 ml. per kg. body weight).

The range of error for single counts of under 1% was $\pm 0{\cdot}3\%$, and for counts over 1% was $\pm 0{\cdot}15\%$. The maximum rise in the reticulocyte count in the period following the venesection was taken as an index of the magnitude of the erythropoietic response, but as the reticulocyte count in rabbits normally shows a seasonal variation of 0·6 to 2·0%, no change of less than 3% was considered to be significant. Twelve rabbits were bled and the citrated blood was re-injected; in 8 the reticulocyte count increased significantly within 10 days. When the blood withdrawn was replaced by an equal volume of citrated normal saline, in 5 out of 6 rabbits the same result was obtained, although an intravenous infusion of citrated saline without previous venesection was without effect on the reticulocytes. Venesection and simultaneous transfusion with an equal volume of citrated blood from another rabbit did not result in reticulocytosis. From these findings the author concludes that oxygen lack, rather than a change in the circulatory blood volume, is the cause of the erythropoiesis.

Transection of the spinal cord at the level of C 7 did not affect the reticulocyte count in 2 control animals. Following venesection, 4 out of 5 rabbits showed an increase in circulating reticulocytes within 5 days. In 4 experiments on coelioparabiotic pairs of rabbits, in which the maximum reticulocyte level was normally 4%, venesection of one member of the pair resulted within 8 days in a parallel reticulocytosis in both members. A significant increase in reticulocyte count within 3 to 5 hours resulted from bilateral constriction of the carotids for 10 to 15 minutes, and clamping of the splenic artery led to a reticulocytosis within 24 hours. No significant change in reticulocyte count occurred when the hepatic or thyroid arteries were compressed. Ligation of the splenic veins did not prevent the usual response to venesection carried out 3 hours later. An injection of a sclerosing solution around the vessels in the splenic hilum caused a slight but definite reticulocytosis in 8 out of 9 rabbits within 10 days.

In a discussion of these experimental findings, together with a survey of the literature, the author postulates the existence in rabbits of a specific erythropoietic hormone acting on the bone marrow, the hormone being produced in the reticulo-endothelial system, especially the spleen, in response to oxygen lack. A rapid response, taking effect within a few hours, is produced by the action of severe oxygen lack on a specific centre in the mid-brain, from which the reticulo-endothelial system is influenced through the spinal cord and splanchnic nerves. A slower response, taking a few days to develop and of undetermined mechanism, is the principal reaction to a moderate haemorrhage. *M. Lubran*

Pharmacology and Therapeutics

471. **The Absorption and Excretion of Rutin and Related Flavonoid Substances**
W. G. CLARK and E. M. MACKAY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 1411–1415, Aug. 19, 1950. 41 refs.

The Council on Pharmacy and Chemistry of the American Medical Association has accepted this report for publication, as a stimulus to further investigation of possible significant effects of rutin and related substances when given by mouth.

The report details the tests used for qualitative and quantitative estimation of the substances examined, which included rutin, its soluble complexes with methyl glucamine and methenamine, " methylated hesperidin chalcone ", the sodium salts of esculetin-4-carboxylic acid and of quercetin-6′-sulphonic acid, " calcium flavonate glucoside ", " citrin ", gossypin, and xanthorhammetin. Tests in human subjects after an oral dose of 50 mg. of substance per kg. showed that urinary excretion of these substances was negligible and that none was recoverable from the faeces. *In vitro* incubation studies showed that rutin is destroyed by aqueous suspensions of faeces. In rats, negligible proportions of the compounds were absorbed from the intestine or excreted in the urine, but some of them were recovered almost completely from the lower bowel. Because of the limitation of the analytical methods " it cannot be said that very minute quantities of the flavonoids were not absorbed ".

The evidence supports that already accumulated. It is unlikely that the substances are vitamin-like or that they have any specific chemical or therapeutic effects. Brief mention is made of some experiments reported to the American Physiological Society which show that, when given by injection, these substances may elicit a non-specific stress or " alarm reaction ", which may explain many of their reputed effects.

Derek R. Wood

472. **The Comparative Absorption of Vitamin A from a Water-miscible and an Oily Preparation by Normal Human Adults and Patients with Steatorrhea**
B. C. BARNES, E. E. WOLLAEGER, and H. L. MASON. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 982–987, Aug., 1950. 1 fig., 23 refs.

A comparative study was made at the Mayo Clinic of the intestinal absorption of vitamin A from a water-miscible and from an oily preparation in normal adults and patients suffering from non-tropical steatorrhoea. The experiment was started after the subjects had undergone preliminary saturation with the water-miscible vitamin preparation so as to ensure the presence of adequate liver stores of the vitamin. Each subject then took by mouth 7,500 i.u. of vitamin A per kg. body weight in the oily preparation and, in a second test 72 hours later, the same dose in the form of the water-miscible preparation. Before, and for 72 hours after, each dose the blood level and faecal and urinary excretion of vitamin A were estimated. In all the 12 healthy controls the level of vitamin A in the blood was higher after taking the vitamin in aqueous dispersion, and the faecal loss was correspondingly lower, than after the oily preparation. The other group consisted of 6 patients with steatorrhoea, one of whom suffered in addition from diabetes mellitus. In these patients the plasma vitamin-A level rose more rapidly and to a greater height after administration of the water-miscible preparation than after the oily preparation had been given, but in each case the curve was abnormally low compared with those of the controls, except in the case of the diabetic subject, whose absorption curve after ingestion of the watery preparation was normal. In all 6, however, faecal loss was abnormally high with both preparations.

It is concluded that gastro-intestinal absorption of vitamin A is facilitated by emulsifying the vitamin in water and that the estimation of the faecal vitamin content is sometimes necessary in order to get an accurate measure of vitamin-A absorption in patients with sprue. Finally, previous observations were confirmed that there is not significant loss of vitamin A in the urine, even when large doses of the vitamin are given and high blood concentrations obtained. *A. I. Suchett-Kaye*

473. **The Anticonvulsant Effect of Procaine.** (Über die Beeinflussung der Krampferregbarkeit des Zentralnervensystems durch Novocain)
N. GERLICH. *Archiv für Experimentelle Pathologie und Pharmakologie* [*Arch. exp. Path. Pharmak.*] **210**, 311–316, 1950. 5 figs., 12 refs.

The central action of procaine was investigated by observing its effect on electrically-induced convulsions in guinea-pigs. Procaine solution (5%) injected subcutaneously in doses of 75 to 150 mg. per kg. body weight had a depressant effect on the convulsions produced in these animals, but the effect did not last long. The alteration in the type of convulsion was the same as that produced by phenobarbitone; with high doses (150 mg. per kg.) the clonic phase was almost completely abolished. The combination of procaine with phenobarbitone had an additive effect. *R. Wien*

474. **The Effect of Some Derivatives of Polamidon.** (Über die Wirkung einiger Derivate des Polamidons)
F. HERR and J. PÉRSZÁSZ. *Archiv für Experimentelle Pathologie und Pharmakologie* [*Arch. exp. Path. Pharmak.*] **210**, 294–304, 1950. 1 fig., 16 refs.

Since the discovery of pethidine a search has been made for other analgesic compounds which have a less depressant action than morphine. Of 12 compounds, all derivatives of " hexalgon ", whose analgesic properties

were examined in mice, only hexalgon itself (1-piperidino-3 : 3-diphenyl-hexan-4-on hydrobromide) and "polamidon" (2-dimethylamino-4 : 4-diphenyl-heptan-5-on) had an analgesic action comparable with that of morphine. Polamidon was the more potent analgesic, a dose of 5 mg. being equivalent to 7 mg. of morphine, 10 mg. of hexalgon, or 35 mg. of pethidine per kg. body weight. Both compounds were more toxic than morphine, the lethal doses of morphine, polamidon, and hexalgon by subcutaneous injection into mice being 450, 120, and 140 mg. per kg. respectively. The effect on respiration was measured in rabbits, the respiratory rate and minute volume being determined with and without the addition of carbon dioxide. All the compounds had a depressant effect on respiration, but that of hexalgon was the least, a dose of 5 mg. per kg. diminishing the respiratory minute volume by 26·8%, compared with 31·7% for polamidon and 46% for morphine. The compounds did not have any emetic action in dogs, and they counteracted the emetic action of apomorphine. They had a spasmolytic effect against pilocarpine contractions of the isolated intestine of the rabbit, 12·5 μg. of polamidon or hexalgon having a greater effect than 30 μg. of papaverine. In cats under urethane anaesthesia the intravenous injection of polamidon and hexalgon caused a transitory fall in blood pressure. *R. Wien*

475. **Measurement of Pathological Pain in Distinction to Experimental Pain**

A. S. KEATS, H. K. BEECHER, and F. C. MOSTELLER. *Journal of Applied Physiology* [*J. appl. Physiol.*] **3**, 35–44, July, 1950. 4 figs., 6 refs.

This is an account from the anaesthesia laboratory of the Harvard Medical School of the method developed there in the past 3 years for determining the analgesic potency of drugs. The subjective responses of patients suffering post-operative pain are used, rather than any of the methods devised for producing and measuring pain experimentally. Relief of naturally occurring pain is considered to be a better criterion of analgesic activity. Both perception of painful stimuli and the psychic modification of these stimuli are concerned in the phenomenon of natural pain. The authors believe that, in experimental pain, probably only the changes in perception of painful stimuli are measured.

In principle, the method involves giving repeated injections of two drugs alternately to each subject in groups of 25 to 30 patients during the 30 hours after a major surgical procedure which is considered likely to cause persistent and severe pain. The other essential conditions are absence of any contraindication to morphine or barbiturate administration, and sufficient intelligence and orientation of the patient. Morphine was used as the standard drug in a dose of 10 mg. per 150 lb. (67·5 kg.) body weight. The identities of the drugs given were unknown to patients, nurses, and technicians. Technicians who visited the patients before the drugs were injected and 45 and 90 minutes later, classified the response as "relief" or "no relief". "Relief" was defined as disappearance of "most" or "more than half" of the pain. If "relief" was reported both 45 and 90 minutes after a dose, the latter was regarded as an analgesic dose. The percentage relief—ratio of number of analgesic doses to total number of doses given—represents the analgesic potency. A high correlation was found between the total number of doses received and the number ineffective in any patient, indicating that in those given the largest number of doses the pain was of greatest intensity and duration. The use of the total number of doses as an index of the order of pain is thus justified. The order of pain appeared to be independent of sex, personality type, disease, or surgical procedure. The use of two drugs in each patient during the same period serves for control of all patient-to-patient variables.

An illustration is given of the use of the method. Patients received alternately injections of the standard dose of morphine and of a different dose of morphine as an unknown. The dose–response curve tended to become asymptotic just beyond the morphine standard line but, on assuming a linear relation for the lower part of the curve, it was found that 10·8 mg. of unknown (morphine) had analgesic activity equal to that of 10 mg. of morphine. Other results are to be described elsewhere. Some other interesting figures are given which illustrate both the variation in intensity of clinical pain and also the differential sensitivity to morphine analgesia in man. The percentage relief is plotted as a frequency distribution, figures being obtained from 42 small groups of patients, 11 to 22 patients in each group receiving 17 to 34 doses of morphine. In these groups relief ranged from 55 to 94% with a mean of $75{\cdot}5 \pm 8{\cdot}9\%$. This indicates the wide variation in the response to morphine, which is a resultant of the sensitivity to analgesia and the intensity of the pain. The wide range observed with groups of 11 to 22 patients emphasizes the danger of comparing small groups of differing patients.

[A comparison of the analgesic effects of morphine and pentobarbitone by this method is described in *J. Pharmacol.*, Sept. 1950, **100**, 1. The use of this method may resolve some of the apparent anomalies which have been reported with the other methods involving experimental pain in animals or man. The original paper must be consulted for the precise details.] *Derek R. Wood*

476. **The Choleretic Potencies of Some Synthetic Compounds**

M. J. GUNTER, K. S. KIM, D. F. MAGEE, H. RALSTON, and A. C. IVY. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **99**, Part 1, 465–478, Aug., 1950. 2 figs., 17 refs.

A series of 145 synthetic compounds were tested for choleretic action in dogs. Bile was collected from the cannulated common bile duct and the amount measured at half-hourly intervals. When the volume was constant, 0·05 millimol of dehydrocholic acid per kg. was administered intravenously in two minutes. When the effect had worn off (about 90 minutes later), a similar dose of the drug under test was given intravenously, and the total volume of the first sample collected was compared with the volume of the first collection resulting from dehydrocholic-acid administration. All the potent compounds produced a fall in blood pressure immediately after injection. Naphthols possessing both a methoxy or

hydroxy group and a β-ketopropionic or a keto-acrylic-acid side chain were found to be potent, as also were acenaphthols with β-ketopropionic acid, acrylic acid, or keto-acrylic-acid side chains. A hydroxy-β-ketopropionic-acid derivative of *cyclo*hexylbenzene was also found to be potent. No single-ring or straight-chain compounds were placed amongst the twelve of greatest potency. *G. B. West*

477. **Multiple-balloon Kymographic Recording of the Comparative Action of Demerol, Morphine and Placebos on the Motility of the Upper Small Intestine in Man**
W. P. CHAPMAN, E. N. ROWLANDS, and C. M. JONES. *New England Journal of Medicine* [*New Engl. J. Med.*] **243**, 171–177, Aug. 3, 1950. 5 figs., 12 refs.

By means of a multiple-balloon water-manometer system the effects of giving pethidine (" demerol "), morphine, and inert placebos on the motor activity of the small intestine were studied in 8 subjects without gastro-intestinal disease. The subcutaneous administration of 100 mg. of pethidine had effects qualitatively similar to, but quantitatively less marked than, those following the administration of 10 mg. of morphine by the same route, the action of morphine being that commonly described in the literature. The administration of placebos had no constant effects. *P. Mestitz*

478. **The Anticholinesterase Activity *in vitro* of the Insecticide Parathion (*p*-Nitrophenyldiethyl Thionophosphate)**
D. GROB. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **87**, 95–105, Aug., 1950. 2 figs., 15 refs.

The activity of " parathion " as an inhibitor of cholinesterase was compared with that of tetraethyl-pyrophosphate, di*iso*propylfluorophosphonate, and neostigmine. Its activity is less and its action slower than that of any of these compounds. Mixtures of parathion and esterase regain some part of esterase activity on dilution or on dialysis, provided that this takes place within a few hours, at any rate within 9 hours. Although the activity of parathion is less than that of the other compounds *in vitro*, it differs very slightly from them in toxicity *in vivo* and it is suggested that factors other than anticholinesterase activity may be involved. Parathion is much less soluble in water and more soluble in lipids than are the other compounds examined.
V. J. Woolley

479. **Studies on Physiologic Effects of Large Doses of Epinephrine**
I. M. VAGRAN and H. E. ESSEX. *American Journal of Physiology* [*Amer. J. Physiol.*] **162**, 230–242, July, 1950. 2 figs., 19 refs.

The toxic action of intravenous injections of adrenaline (epinephrine) and the development of tolerance to the drug on repeated injection were studied.

The minimal lethal doses (M.L.D.) and " surely lethal doses " (S.L.D.) for dogs, rabbits, and guinea-pigs injected in 10 seconds were determined. The M.L.D. for dogs was 0·1 mg., for rabbits 0·05 mg., and for guinea-pigs 0·1 mg. per kg. body weight; the corresponding figures for S.L.D. were 0·8 mg., 0·45 mg., and 0·4 mg. per kg. If the adrenaline was injected more slowly, tolerance was greater.

Repeated injection of the drug increased the tolerance. Thus two dogs survived a course of 30 injections over 107 days, starting with a dose of 0·1 mg. per kg. and ending with a dose of 3·0 mg. per kg. Small dogs tolerated large doses of adrenaline better than did large dogs. That the tolerance is not due to an antihormone present in the blood was shown as follows. Two dogs, one of which had received a series of injections, were bled out and the blood of each was transfused to the other. After 24 hours an injection of 1·5 mg. per kg. was given to both animals. The dog which had been previously injected tolerated this dose but the other died in shock.

During the injection of adrenaline a number of toxic symptoms, such as vomiting, nasal discharge, and erection of the hair, appeared. In dogs repeatedly injected these signs appeared reflexly when the dog was placed on the table before injection started.

By using transparent chambers inserted into the ear, prolonged stasis of the circulation in the small blood vessels was observed during the injection of adrenaline. It is argued that adrenaline shock is due to prolonged anoxia of the tissues. *R. P. Foggie*

480. **Influence of Antihistaminics on Respiratory Response to Hypoxia**
W. L. BURKHARDT, B. R. EASTMAN, and H. B. HALE. *Journal of Applied Physiology* [*J. appl. Physiol.*] **3**, 29–34, July, 1950. 3 refs.

Following a report that mice treated with an antihistamine substance did not show the usual increase in respiratory rate when later exposed to low oxygen tension, the authors performed similar experiments on dogs with a variety of antihistamine drugs. The problem is important because of the implication that altitude tolerance may be diminished in flying personnel, who are taking antihistamine drugs for therapeutic reasons.

Through a tracheal cannula, the respiratory rate and minute volume were recorded in dogs anaesthetized with sodium pentobarbitone. Observations were made of the effect of changing the breathing mixture from air to mixtures of nitrogen and oxygen containing 7 to 12% of oxygen. The increases in respiratory rate and minute volume which occurred after changing to the mixtures of low oxygen tension were compared, under normal conditions and after injection of an antihistamine drug. These responses to hypoxia were insignificantly altered by 10 or 100 mg. of tripelennamine (" pyribenzamine "), 100 mg. of diphenhydramine (" benadryl "), 100 mg. of antazoline (" antistin "), 10 mg. of " dramamine ", or 0·4 mg. of " chlor-trimeton ". Apparently slight reductions in the response after dramamine or chlor-trimeton were insignificant or could not be repeated. It is noted that Liljestrand has recently reported similar findings in cats given " lergitin ".

Incidental confirmation was obtained of the respiratory stimulant action of these doses of antihistamine drugs;

100-mg. doses of tripelennamine, diphenhydramine, and antazoline caused respectively increases of 82%, 44%, and 16% in minute volume. Dramamine had a moderate effect, but 0·4 mg. of chlor-trimeton was ineffective.

Derek R. Wood

481. **Benzylimidazoline ("Priscol"). A Study of its Pharmacology and Clinical Applications.** (La benzyl-imidazoline (Priscol). Étude pharmacodynamique et applications cliniques)
B. ROCH-BESSER. *Helvetica Medica Acta* [*Helv. med. Acta*] Suppl. 27, 1–175, 1950. 12 figs., bibliography.

482. **The Testing of the Effect of Liver Extracts on Pernicious Anaemia by Observations on Lead Anaemia in Rabbits.** (Über die Testung antiperniciös-wirksamer Leberextrakte mit Hilfe der Bleianämie am Kaninchen)
N. GERLICH. *Archiv für Experimentelle Pathologie und Pharmakologie* [*Arch. exp. Path. Pharmak.*] **211**, 90–96, 1950. 3 figs., 6 refs.

A progressive anaemia was induced in 8 male rabbits weighing 1·7 to 3·2 kg., by giving 3 successive daily intravenous injections of lead acetate solution, each containing 5·5 to 6 mg. of the salt per kg. body weight, the lowest erythrocyte count and haemoglobin concentration (50 to 60% of the initial values) being reached in 5 days. Without treatment, complete recovery took place in 4 to 6 weeks.

Three groups, each consisting of 4 animals weighing 2·5 to 3 kg., received intravenous injections of 1 ml. of "campolon", in 1 in 5, 1 in 7, and 1 in 9 dilution respectively, with the lead acetate, a control group of 4 rabbits being injected with lead acetate alone. The 1 in 5 dilution of liver extract prevented appearance of lead anaemia, the 1 in 7 dilution had an inhibitory effect, but the 1 in 9 dilution caused no inhibition. It is suggested that this technique might be employed for estimating the concentration of antipernicious-anaemia factor in liver extracts, varying dilutions being injected with a constant dose of lead acetate and the minimum dose being found which just inhibits lead anaemia. Control experiments with a liver extract of known potency should be carried out at the same time.

M. Lubran

483. **Experimental Study of a New Haemostatic Agent, Sodium α-Naphthylamine-4-sulphonate.** (Étude expérimentale d'un hémostatique: α-naphthylamine-4-sulfonate de sodium (naphthionine S.N.S.))
H. DUBOIS-FERRIÉRE. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **80**, 861–866, Aug. 19, 1950. 7 figs., 5 refs.

A new haemostatic drug, the sodium salt of α-naphthylamine-4-sulphonic acid ("naphthionine"), is stated to be well tolerated when given intravenously or intramuscularly; even in large doses it does not cause thrombosis or histological changes in the tissues. It is quickly eliminated in the urine (up to 75% within 2 hours) and is almost completely excreted within 8 hours. This new compound was evolved from a consideration of the formula of Congo red. Some workers think that the effect of naphthionine is due to alteration of the protein iso-electric point and stimulation of the reticulo-endothelial system, causing a transfer of fibrinogen into the circulation with an increase of thromboplastin in the blood.

The haemostatic action of the compound was studied in the rabbit, the dog, and in man. In rabbits, after the intramuscular injection of 1 ml. of a 10% solution per kg., the bleeding time was reduced within 1½ hours from 4 minutes 20 seconds to 1 minute 47 seconds, and the coagulation time from 2 minutes 21 seconds to 49 seconds. The maximum effect occurred at 1½ to 3 hours and recovery did not take place for more than 8 hours. In 18 normal human subjects after the intramuscular injection of 10 ml. of a 10% solution there was no alteration in haemoglobin level or in the blood picture, while the bleeding time after 1½ hours was reduced from 1 minute 30 seconds to 57 seconds and the coagulation time from 11 minutes to under 6 minutes.

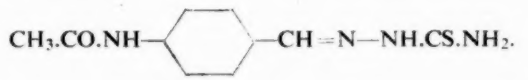
R. Wien

484. **Chronic Toxicity of Thiomerin Compared to Other Mercurial Diuretics**
R. T. CAPPS, F. L. KOZELKA, and O. S. ORTH. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 511–514, July, 1950. 14 refs.

CHEMOTHERAPY

485. **Clinical and Experimental Studies on the Effect of Thiosemicarbazones.** (Klinische und experimentelle Studien zur Thiosemicarbazonwirkung)
O. KOCH and G. STÜTTGEN. *Archiv für experimentelle Pathologie und Pharmakologie* [*Arch. exp. Path. Pharmak.*] **210**, 409–423, 1950. 4 figs., 18 refs.

The histaminase activity of the blood was determined during chemotherapy of tuberculosis. The compound employed was the thiosemicarbazone, "TB I/698", 4-acetylaminobenzaldehyde thiosemicarbazone:



Histaminase was prepared from defibrinated venous blood, and its activity determined by its ability to inactivate graded concentrations (0·2 to 1·6 μg.) of histamine, tested on atropinized guinea-pig intestine.

In 10 patients not suffering from tuberculosis the histaminase activity was remarkably constant (1·4) with a variation not greater than 10%. In a series of 23 tuberculous patients treated with the drug in amounts varying from 0·175 to 18,525 g. over 4 to 207 days, the histaminase-activity values of the blood fluctuated from 0 to 1·4. It was concluded from these results that the blood histaminase level was lowered in these cases during the first 3 to 14 days of treatment. Graphs are, however, shown of the blood histaminase activity in 4 patients apparently unaffected by treatment. An early lowering of histaminase activity is interpreted as favourable, otherwise the prognosis is not so good. Other experi-

mental work was carried out with " TB VI ", a water-soluble thiosemicarbazone derivative, the constitution of which is not stated. *R. Wien*

486. **Potentiation of the Antimalarial Activity of Sulfadiazine by 2 : 4-Diamino-5-aryloxypyrimidines**
J. GREENBERG and E. M. RICHESON. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **99**, 444–449, Aug., 1950. 16 refs.

Certain 2 : 4-diaminopyrimidines have been shown to have antimalarial activity and, like proguanil, to antagonize pteroylglutamic acid. The present work shows that two compounds, 2 : 4-diamino-5-(*p*-chlorophenoxy)-pyrimidine and 2 : 4-diamino-5-(*p*-chlorophenoxy)-6-methylpyrimidine, also share with proguanil the property of potentiating the antimalarial action of sulphadiazine against *Plasmodium gallinaceum in vivo*. One-quarter of the minimum effective dose of either of the diaminopyrimidines plus one-sixteenth of the minimum effective dose of sulphadiazine had an effect equal to the full minimum effective dose of sulphadiazine. Twenty other compounds, including a wide range of active antimalarials, had no such synergistic effect when given with sulphadiazine. It is concluded that the 2 : 4-diaminopyrimidines and proguanil interfere in the metabolic pathways mediated by pteroylglutamic acid in a similar manner. However, their modes of action are not identical, because antagonism to pteroylglutamic acid and antimalarial activity do not run parallel; also, a proguanil-resistant strain of *P. gallinaceum* does not show cross-resistance to 2 : 4-diamino-5-(*p*-chlorophenoxy)-6-methylpyrimidine. *L. G. Goodwin*

ANTIBIOTICS

487. **Bacteriologic Studies of the Newer Antibiotics: Effect of Combined Drugs on Microorganisms**
S. SPICER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 183–191, Aug., 1950. 15 refs.

Penicillin, streptomycin, dihydrostreptomycin, chloramphenicol, aureomycin, and bacitracin were each tested against strains of haemolytic streptococci, *Streptococcus viridans*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Haemophilus influenzae*, *H. pertussis*, and pneumococci which were known not to have been in contact with antibiotic drugs. Bacterial sensitivity was measured by the size of the zone of inhibition produced on a seeded plate by a paper disk impregnated with a solution of the antibiotic, and also by determining the number of residual viable organisms to be obtained from the disk by washing with broth.

All antibiotics left a residuum of viable organisms and the number of such organisms was regarded as a better index of sensitivity than the size of the zones of inhibition. By its use, penicillin G was shown to be more potent than penicillin K (as found by clinical experience). Against Gram-positive organisms penicillin was the most effective, bacitracin the next, and aureomycin the least effective. Aureomycin was also the least effective against Gram-negative organisms. Chloramphenicol was the most effective against *H. influenzae* and *H. pertussis*, while streptomycin was the most active against *K. pneumoniae*. In the case of penicillin, bacitracin, aureomycin, and chloramphenicol the residual organisms were still sensitive to the respective antibiotics, but in the case of streptomycin and dihydrostreptomycin they were resistant.

The effects of penicillin paired with chloramphenicol and aureomycin respectively, and of streptomycin paired with penicillin, chloramphenicol, and aureomycin respectively were determined on the test strains. When organisms were sensitive to both antibiotics, the combined response was additive, but if the organism was insensitive to one of the drugs, then the effect of the other was impaired. The synergistic effect is explicable as due to each drug acting on the viable residuum left by the other, while it is suggested that the interfering action is due to the stimulating effect of the ineffective drug on the organism sensitive to the other drug.
M. Lubran

488. **Chemoprophylactic Effectiveness of Aureomycin and Terramycin in Murine Bartonellosis**
M. F. STANTON, L. LASKOWSKI, and H. PINKERTON. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 705–707, Aug., 1950. 4 refs.

Two strains of white rats were used in these experiments, one of which was bartonella-free and the other a " carrier " strain latently infected with *Haemobartonella muris*.

In the first experiment the spleen was removed from 19 bartonella-free rats and 3 weeks later they received an injection of 1 ml. of rat blood containing *H. muris* of high virulence. Twenty-four hours later 5 began to receive aureomycin, 4 terramycin, and 5 chloramphenicol; 5 served as controls. All 5 control rats died and 4 out of 5 rats receiving suspensions of chloramphenicol died 5 to 7 days later. None of the rats receiving aureomycin or terramycin showed clinical evidence of anaemia or haematuria, although 2 in the aureomycin group died of unknown causes on the 20th and 21st days.

In the second experiment 30 carrier rats underwent splenectomy; 24 hours later 10 began to receive aureomycin and 10 terramycin, 10 being left as controls. All the controls became severely ill, and 5 of them died between the 6th and 9th days. The 20 treated animals survived without showing clinical evidence of illness.
A. W. H. Foxell

489. **The Action of Aureomycin and other Chemotherapeutic Agents in Experimental Brucellosis**
A. I. BRAUDE and W. W. SPINK. *Journal of Immunology* [*J. Immunol.*] **65**, 185–199, Aug., 1950. 7 figs., 14 refs.

Subcutaneous injection of aureomycin hydrochloride (0·4 mg. given in 2 doses daily, each in a total volume of 0·5 ml.) delays death and reduces the total mortality in mice infected intraperitoneally with 10^{10} *Brucella abortus* suspended in saline or in 5% gastric mucin. The protective effect is evident if the drug is first given at the time of infection and persists for at least 72 hours after the last

dose of drug. Simultaneous administration of streptomycin (0·4 mg. twice daily) and sulphadiazine (0·8 mg. twice daily) had a similar but slightly less marked effect. Chloramphenicol had little effect in the highest practicable doses. When mice were infected with sublethal doses of *Br. abortus*, aureomycin appeared to reduce the number of *Br. abortus* recoverable from their organs compared with those recovered from untreated controls. Similar results were obtained in aureomycin treatment of guinea-pigs infected with *Br. abortus* and *Br. suis*; in the latter infection aureomycin treatment appeared to reduce the number and size of the abscesses formed. Guinea-pigs are, however, relatively so susceptible to aureomycin poisoning that experiments on its protective capacity were very difficult to carry out. *C. L. Oakley*

490. **Sensitivity to Aureomycin. Report of a Case**
F. BURSTEIN. *American Journal of Ophthalmology* [*Amer. J. Ophthal.*] **33**, 973–974, June, 1950. 3 refs.

A patient treated with aureomycin for a bilateral staphylococcal conjunctivitis developed swelling of the eyelids, itching, and a transient urticaria of the scalp, back, and forearms, with exacerbation of acne rosacea lesions on the face. These symptoms disappeared on cessation of treatment. The aureomycin was made up as drops of 25 mg. aureomycin hydrochloride with 25 mg. sodium borate and 62·5 mg. of sodium chloride freshly dissolved in 5 ml. of distilled water. *E. S. Perkins*

491. **Neurotoxic Reactions to Dihydrostreptomycin**
D. T. CARR, H. A. BROWN, C. H. HODGSON, and F. R. HEILMAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 1223–1225, Aug. 5, 1950. 1 fig., 4 refs.

Of 35 patients treated for various conditions with dihydrostreptomycin, 10 subsequently showed some evidence of damage to vestibular or auditory function. Clinical details of these 10 cases are given and the conclusion is drawn that the toxic reactions were due to overdosage, or impaired renal function, or both. In the authors' experience a serum concentration of more than 60 mg. of the drug per ml. is likely to cause toxic effects, and a dosage of more than 1 g. of dihydrostreptomycin in 12 hours is likely to produce such a serum concentration. *E. A. Brown*

492. **Effect of 3-Hydroxy-2-phenylcinchoninic Acid on Renal Secretion of Phenyl Red and Penicillin**
C. G. ZUBROD, E. H. DEARBORN, and E. K. MARSHALL. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 671–674, Aug., 1950. 15 refs.

" Carinamide " (or 4′-carboxyphenylmethanesulphonanilide) blocks the tubular secretion of phenyl red and penicillin; 3-hydroxy-2-phenylcinchoninic acid has been shown to suppress the excretion of phenyl red by the kidney, and experiments reported in this paper indicate that it has a similar action on the excretion of penicillin in dogs. This action is attributed to a blocking of the renal tubular secretory mechanism. *A. W. H. Foxell*

493. **On Penicillin Inactivators and Susceptibility of Micro-organisms to Penicillin**
J. W. CZEKALOWSKI. *Edinburgh Medical Journal* [*Edinb. med. J.*] **57**, 281–304, 1950. Bibliography.

[This monograph is based on the available data from the literature up to 1949, and deals with penicillin inactivators of organic and inorganic origin, as well as with the factors influencing the production and activities of penicillinase. Reference is also made to the susceptibility of micro-organisms to penicillin.]

494. **Investigation of Penicillin Preparations and Dosage Schedules.** (Undersøgelser af penicillinpraeparater og doseringsmåder)
K. A. JENSEN, P. J. DRAGSTED, P. MØLLER, and I. KIÆR. *Ugeskrift for Læger* [*Ugeskr. Læg.*] **112**, 1043–1046, July 27, 1950. 2 figs., 6 refs.

Manufacturers' statements on the levels of penicillin in the blood after injection of their particular brands of procaine penicillin must be treated with caution. The authors show that concentrations may vary greatly in different subjects, and that high values may be due to the presence of heart or kidney disease. Urinary clearance was proportional, in their experiments, to the blood concentrations obtained at the corresponding times. *W. G. Harding*

SULPHONAMIDES

495. **Erythema Nodosum in Association with Sulphathiazole in Children. A Clinical Investigation with Special Reference to Primary Tuberculosis.** [In English]
S. I. ROLLOF. *Acta Tuberculosea Scandinavica* [*Acta tuberc. scand.*] **24**, Suppl. 24, 1–215, 1950. Bibliography

Past investigations into, and present views on, the aetiology of erythema nodosum are reviewed. In the present investigation 706 cases were examined, 231 being tuberculous and 475 non-tuberculous. Of the non-tuberculous patients 98 had received B.C.G. vaccine and were tuberculin-positive, the remainder being tuberculin-negative; all 475 patients had had some other infection for which they were treated with sulphathiazole.

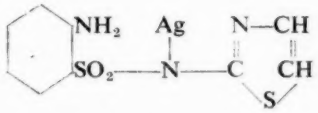
Sulphathiazole erythema nodosum occurred in 129 cases, of which 105 were tuberculous and 24 non-tuberculous. It occurred in 45·5% of tuberculous cases and in 5·1% of non-tuberculous; the difference is statistically significant. The incidence of erythema nodosum in cases of primary tuberculosis was higher when sulphathiazole was administered, either therapeutically or experimentally; this also was statistically significant. The frequency of sulphathiazole erythema nodosum was inversely proportional to the age of the tuberculous process; the more recent the process, the higher the frequency of sulphathiazole erythema nodosum. It was impossible to conclude with certainty that there was a relation between the development of sulphathiazole erythema nodosum and either the activity of the tuberculous process or the presence of " multiple infection ", such as β-haemolytic streptococci in the throat. There was no evidence that erythema nodosum was the result of

hypersensitivity to sulphathiazole. In some cases sensitivity to this drug could be ruled out. The rapid onset of sulphathiazole erythema nodosum, especially in cases where no sulphonamide had previously been administered, suggested that the mechanism was different from that in ordinary drug rashes. Erythema nodosum can develop in association with one of the other sulphonamides, but the frequency, in comparison with sulphathiazole, is very low. Generalized exanthemata may occur with any of the sulphonamides.

No absolute diagnostic difference was observed between the lesions of spontaneous erythema nodosum and those of sulphathiazole erythema nodosum. The lesions of sulphathiazole erythema nodosum cleared up rapidly when the drug was stopped, without passing through the colour phases often seen in the spontaneous type. There was no evidence that erythema nodosum is a specific disease. The investigation indicated that spontaneous erythema nodosum and sulphathiazole erythema nodosum were manifestations of an allergic phenomenon due to some kind of infection.—[From the author's summary.]

496. **Treatment of Dysentery with a Colloidal Preparation of a Silver Salt of Sulphathiazole.** (Лечение дизентерии коллоидно-дисперсным препаратом серебряной соли сульфатиазола)
A. F. Bilibin and R. P. Komolova. Клиническая Медицина [*Klin. Med., Mosk.*] **28**, No. 8, 41–44, Aug., 1950.

The authors have introduced a new drug " kdiserssul " (a colloidal silver salt of sulphathiazole) in the treatment of dysentery. Its formula is



They think that the sulphonamide part of the drug is valuable in dealing with the organisms causing dysentery, and the colloidal silver valuable in dealing with the secondary infection usually present in all cases of dysentery.

Kdiserssul, 100 ml. of a 1 or 2% solution in boiled water, was given as an enema through a proctoscope or a catheter into the rectum or sigmoid. This was done on 3 consecutive days and repeated if necessary. After the first course abdominal pain and tenesmus usually ceased, and the mucous membrane of the rectum and sigmoid often became normal.

Of 239 cases treated 192 were acute and 47 chronic cases. Among the latter, 7 patients had been ill for 1 year, 19 for 2 to 3 years, 2 for 4 to 6 years, and 10 for over 6 years. Most patients were middle-aged; there were 4 children aged 2 to 4 years and 12 persons over 60 years of age. In 97 cases the treatment was started during the first five days of illness. After treatment of 192 cases of acute dysentery 8 still showed ulceration and inflammation of the rectum and sigmoid. Of 47 cases of chronic dysentery 4 showed pathological changes in the rectum and sigmoid. Amongst 54 controls 32 were considered still to be ill after other methods of treatment had been tried. Of all acute dysentery cases two-thirds were clinically and anatomically cured after 3 to 6 kdiserssul treatments; amongst the chronic cases 9 were cured after 3, 14 after 6, 15 after 9, and 5 after 10 kdiserssul treatments. In 2 cases the condition remained unchanged even after repeated courses of treatment. In 2 chronic cases relapse occurred after one year, but another course brought complete clinical and anatomical cure. No toxic effects were noted. The drug could also be used in combination with other methods of treatment.

The authors emphasize that the time of observation is too short for evaluation of the efficiency of the drug, and that clinical and anatomical cure does not always go parallel with complete destruction of all organisms causing dysentery. *N. Chatelain*

497. ***In vitro* Sensitivity of Bacteria to Sulfonamide Combinations as Compared to Single Sulfonamides**
F. B. Schweinburg and A. M. Rutenberg. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 480–483, July, 1950. 14 refs.

Several therapeutic advantages are claimed for mixtures of sulphonamides; for example, it is said that a mixture is as effective as the same weight of a single sulphonamide, and there may even be potentiation of antibacterial effect. To test this statement the sensitivity *in vitro* of 26 Gram-positive and 44 Gram-negative micro-organisms to individual sulphonamides and mixtures of the drugs was determined.

It was found that in 21 of the 70 strains tested some additive or potentiating effect occurred, and of these 21, 19 were Gram-positive cocci. In the case of 42 of the 44 Gram-negative organisms there was no such effect. If it be true that sensitivity to a drug *in vitro* is a good measure of therapeutic potency, the experiments show that the effect of a mixture in any individual case is not predictable, since different strains vary considerably in their response; hence the use of mixtures in preference to single sulphonamides *in vivo* should be controlled by sensitivity tests. In the case of infections with Gram-negative micro-organisms it seems unlikely that any benefit at all would be obtained from the use of sulphonamide mixtures. *E. A. Brown*

TOXICOLOGY

498. **Mercury and Lead Storage in Human Tissues. With Special Reference to Thrombocytopenic Purpura**
E. M. Butt and D. G. Simonsen. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **20**, 716–723, Aug., 1950. 6 refs.

The mercury content of liver and kidney tissue obtained at necropsy in 134 cases was estimated by means of a dithizone method devised by one of the authors and said to give results which are accurate to within 10 μg. of mercury per 100 g. of wet tissue. The cases are divided arbitrarily into 6 groups, according to the cause of death

and history of therapeutic or other intake of mercury: I. Miscellaneous. No known intake of mercury. II. Cases in which death may have been related to poisoning with a heavy metal (Pb, As, Cu, or Sb), including one case of lead poisoning with terminal acute mercurial nephritis due to application of a mercurial ointment to a skin ulcer. III. Cases of renal failure from various causes, with or without history of contact with mercury. IV. Cases of congestive heart failure treated with mercurial diuretics. V. Cases of other conditions treated with mercurial diuretics. VI. Cases of acute thrombocytopenic purpura, developing in 3 out of 13 cases during treatment with a mercurial diuretic, and with a history of contact with mercury in one further case. The mean of the results and the ratio of the mercury content of the liver to that of the kidney in each of these groups are set out as follows:

Group	No. of Cases	Mercury Content in mg. per 100 g.		Liver/ Kidney Ratio
		Liver	Kidney	
I	69	0·006	0·075	1 : 12
II	11	0·058	0·192	1 : 3·3
III	8	0·105	0·425	1 : 4·1
IV	22	0·757	8·619	1 : 11·3
V	11	0·659	3·171	1 : 4·8
VI	13	0·287	0·704	1 : 2·4

In the 13 cases of fatal acute thrombocytopenic purpura the lead content of the liver and kidney was 0·127 mg. and 0·227 mg. per 100 g. respectively. The authors comment on the unusually high levels of mercury found in the cases of thrombocytopenic purpura not associated with treatment with mercurial diuretics. They infer that mercury may have a poisonous effect on germ cells.

A. Michael Davies

499. **The Influence of Beryllium and its Compounds on Man.** (De invloed van beryllium en zijn verbindingen op de mens)

R. FRANT. *Nederlandsch Tijdschrift voor Geneeskunde* [*Ned. Tijdschr. Geneesk.*] **94**, 1474–1480, May 27, 1950.

The light metal beryllium is becoming important in industry in Holland. It is used in the manufacture of fluorescent tubes. Acute irritation of the skin and mucous membranes is known to be caused by beryllium-containing vapours. Removal of the patients from the area of exposure is sufficient for cure. Implantation of small beryllium particles in the skin causes the development of subcutaneous granulomata and ulcers, which require excision. The inhalation of beryllium-containing fumes produces acute interstitial pneumonitis with pyrexia, dyspnoea, cyanosis, and pain in the chest. Though the prognosis is favourable, occasionally death occurs through pulmonary oedema. Recovery takes 1 to 4 months. In a small percentage of cases the lung disease becomes chronic and may give rise to a dramatic change in the patient's appearance. Certain " trigger " conditions may cause an acute exacerbation of the chronic pneumonitis. These cases are described as cases of delayed chemical pneumonitis. The chronic fibrosis of the lung finally causes insufficiency of the right ventricle, increasing cyanosis, clubbing of fingers, and enlargement of liver and spleen. The radiographic appearance of the lung varies from a ground-glass appearance to diffusely spread nodules. The histological picture resembles that in sarcoidosis. Treatment with BAL is ineffective. Renal calculi develop in 13% of cases. *F. Bloem* (*Excerpta Medica*)

500. **Coagulant and Anticoagulant Factors in Snake Venom.** (Principios coagulantes y anti-coagulantes de los venenos de serpientes)

D. DE KLOBUSITZY. *Revista Medica Peruana* [*Rev. med. peruana*] **21**, 425–441, Aug., 1950. Bibliography.

Since 1871, when Fontana first described certain snake venoms as having a coagulant, and others as having an anticoagulant, action on the blood, other investigators have confirmed this finding, but the same venoms have frequently been reported to have opposite effects on coagulability. The present author discusses, among other things, the reasons for these divergent opinions; the conditions in which a coagulant venom becomes anticoagulant; and the therapeutic possibilities of snake venom as a coagulant.

From a review of his own investigations and those of others, he concludes that most venoms contain both coagulant and anticoagulant substances, the effects obtained depending naturally on the relative proportions of these in any given sample; for this reason the effect of a venom on isolated blood components *in vitro* may bear no relation to its effect on whole blood *in vivo*. Another source of confusion lies in the fact that many venoms contain a proteolytic ferment capable of destroying fibrinogen and in this way render the blood non-coagulable, while others destroy prothrombin, also by means of some enzyme. Yet although such venoms are classed as anticoagulants, under special experimental conditions they exert a coagulant effect. In the case of certain types of cobra and other snakes, whose venom contains both coagulant and anticoagulant substances, it has been found both *in vitro* and *in vivo* that the ultimate effect depends on the concentration of venom present—if great, coagulation is impeded, and if small, coagulation is promoted. The presence in snake venom of a specific coagulant factor was first demonstrated by the author and his colleagues who, in 1936, separated from the venom of *Bothrops jararaca* (by fractional precipitation of the neurotoxin) a coagulant substance which they named haemocoagulase, and a similar substance was isolated in 1941 by Rosenfeld and Rubinstein from the venom of *Notochis scutatus*. Temperature seems to play no small part in determining the effect of venoms on the blood; thus whereas the neurotoxin of *B. atrox* of Costa Rica is inactivated at a temperature of 65° C. and that of *B. jararacussu* requires 110° C., their coagulant properties are destroyed at 80° C. and 85° C. respectively. Similarly climate and locality have some effect; thus the venoms of Venezuelan snakes differ profoundly from those of the same species in Central and South American countries.

As regards possible therapeutic applications, Peck and Frank, in 1932, first used small doses of *Ancistrodon piscivorus* venom in the treatment of haemorrhage and since then the venoms of various other species, notably *Vipera russellii*, have been tried for the same purpose. The results in this regard may be epitomized thus: the coagulant components of snake venom may check parenchymatous haemorrhage or capillary bleeding resulting from diminished coagulability of the blood and, in persons with normal coagulability, haemorrhage due to wounds or non-inflammatory tissue destruction; they are useless in haemorrhage of endocrine origin in women. (A very full list of references is appended.)

H. Harold Scott

501. **The Efficacy of Various Thiols as Antidotes to Lewisite**

S. D. SIMPSON and L. YOUNG. *Canadian Journal of Research, E. Medical Sciences* [*Canad. J. Res. (E)*] **28**, 135–142, Aug., 1950. 16 refs.

INDUSTRIAL TOXICOLOGY

502. **Thiocyanate Effect following Industrial Cyanide Exposure. Report of Two Cases**

H. L. HARDY, W. MCK. JEFFRIES, M. M. WASSERMAN, and W. R. WADDELL. *New England Journal of Medicine* [*New Engl. J. Med.*] **242**, 968–972, June 22, 1950. 26 refs.

The authors describe in detail 2 cases of changes in the thyroid in persons exposed to cyanide fumes from the case-hardening process. The highly toxic cyanide ion is rapidly converted in the body to the relatively non-toxic thiocyanate ion, which is excreted irregularly by the kidneys. Persons constantly exposed to cyanide therefore accumulate thiocyanate in the tissues, and it is reasonable to suppose that by interfering with the iodine metabolism this may lead to the development of goitre. There is, in fact, clinical evidence that the treatment of hypertensive patients with thiocyanate may give rise to goitre. It is suggested, therefore, that in the 2 cases reported the goitre was due to thiocyanate accumulation, and further that various symptoms previously attributed to the direct effects of chronic cyanide poisoning may, in fact, be due to this cause, a theory which is well supported by clinical and experimental observations. The authors' purpose in publishing this article is to encourage clinical interest in detoxification mechanisms in the body. *A. Thelwall Jones*

503. **Industrial Poisoning with Nitrochlorobenzol.** (Industriel forgiftning med nitrochlorbenzol)

J. SPAUN. *Ugeskrift for Læger* [*Ugeskr. Læg.*] **112**, 1046–1051, July 27, 1950. 27 refs.

This paper describes the clinical and laboratory findings in 7 young males suffering from chronic industrial poisoning with nitrochlorobenzol. Six were admitted acutely ill, 2 of them direct from their place of work, while in 2 others the onset followed the intake of alcohol. Malaise and cyanosis were present in all cases; other commonly described symptoms and signs, such as headache, giddiness, and pallor, were less constant. The temperature was raised in 3 cases and subnormal in one. Six were mildly anaemic, with haemoglobin values between 81 and 88% (Zeiss); in the seventh the anaemia was more severe (66%). Treatment consisted in the administration of stimulants and oxygen. Most patients could be discharged within one week; five were followed up 6 months later and showed no evidence of after-effects. *W. G. Harding*

504. **Acute Poisoning inside Oil Tanks and its Prevention.** (Ostre zatrucia przy pracach wewnatrz zbiornikow productow naftowych i ich zwalczanie)

J. Z. WALCZYNSKI. *Medycyna Pracy* [*Med. Pracy*] **1**, 60–84, 1950. 33 refs.

The cleansing of oil tanks is dangerous because of the possibility of poisoning; the latter can be avoided by strict application of regulations. Despite the removal of fumes from tanks before the process of cleaning, it should be borne in mind that some vaporized oil derivatives may be left behind.

The author describes 14 cases of acute poisoning which took place during the cleaning of oil tanks and other procedures; the poisoning was due to derivatives of oil. The paper contains details of the pathological findings as well as the clinical symptoms in cases of acute poisoning by oil derivatives. Special attention is paid to the toxicology of benzine poisoning and to safety measures. *J. W. Czekalowski*

505. **Skin Ulcers in a Factory in which Chromium Derivatives were Made.** (Ulceri cutanee in una fabbrica di cromoderivati)

C. L. MENEGHINI. *Rassegna di Medicina Industriale* [*Rass. Med. industr.*] **19**, 161–169, July–Aug., 1950. 3 figs., 10 refs.

It has been suggested that chromate ulceration only occurs when the acid or acid salts are in use and that alkaline chromates do not cause it. The author observed 120 workmen in a factory in which bichromate was used; over 90% had skin lesions. These men had been working for from one month to 18 months, and those most affected were working in the lixiviation or filter departments. A high proportion of the lesions were on the hands, forearms, or feet. The ulcers were rounded or oval and the associated dermatitis, if present, was of the type often described. Sections showed that necrosis was so rapid that little repair had occurred. The author doubts whether any previously existing skin lesion is essential to the development of a chrome ulcer.

He performed numerous experiments which showed that the solution of sodium chromate, sodium aluminate, and ferrous oxide which is obtained after the first stage of purification has a *p*H of about 10 to 10·2. Application of this solution causes ulcers to form on the skin in 6 to 24 hours, and these become very obvious in 48 to 72 hours. The solution of chromate obtained after removal of the other salts is of a yellowish colour, has a *p*H of about 10, and does not readily cause skin lesions when applied. The solution of sodium bichromate obtained by treating the chromate solution with

sulphuric acid, has a *p*H of about 2·8. This solution causes ulceration almost indistinguishable from that caused by the alkaline solutions of chromates. Solutions of chromate and bichromate of equal strength, when applied to the skin, cause typical ulcers in the first case but only mild erythema in the second.

It may be said that alkaline chromates are very harmful, the acid solutions of bichromate are less so, and the dilute and slightly acid bichromate salts cause little or no damage. It appears that some views advanced by earlier authors can no longer be maintained.

Prophylactic measures should include the enclosure of all dangerous processes, the free use of masks, gloves, and protective boots, and the application of weak sulphurous acid to all exposed areas to reduce the chromate to an inactive oxide. Reducing agents should also be used freely in the works to neutralize any noxious material on machines or walls. A water-insoluble barrier cream has proved useful. *G. C. Pether*

506. **Ulceration of Larynx and Vocal Cords in the Manufacture of Chromium Derivatives.** (Ulcerazioni del laringe e delle corde vocali nella fabbricazione di cromoderivati)
G. MANCIOLI. *Rassegna di Medicina Industriale* [*Rass. Med. industr.*] **19**, 170–172, July–Aug., 1950.

The author studied a group of 107 men working at a factory in which sodium bichromate was made, whose ages ranged from 17 to 51 years. They had worked for from 1 month to 20 months in the factory.

Subjective symptoms ranged from local pruritus and burning to sneezing, epistaxis, and rhinorrhoea, the nasal secretion being yellow in colour. Pain was felt in the nose or frontal region; hoarseness, sore throat, and cough were common. Inflammatory changes were seen in the nasal mucosa, and septal perforation was common; a chronic pharyngitis was often seen, with swelling of the cords, ulceration being common on these and on the epiglottis also. The area below the cords was sometimes examined and the upper trachea was seen to be red and oedematous.

The working sites were often covered by a yellowish dust, and the air was dusty and sometimes full of fumes. Although the works were not crowded, the methods of exhaust ventilation were inadequate to prevent gross contamination of the personnel. *G. C. Pether*

507. **Acute Inhalation Toxicity of Beryllium. 1. Four Definitive Studies of Beryllium Sulfate at Exposure Concentrations of 100, 50, 10 and 1 mg. per Cubic Meter**
H. E. STOKINGER, G. F. SPRAGUE, R. H. HALL, N. J. ASHENBURG, J. K. SCOTT, and L. T. STEADMAN. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg. occup. Med.*] **1**, 379–397, April, 1950. 7 figs., 20 refs.

Experimental production of the acute reaction to inhalation of beryllium compounds is reported. Methods are described in detail for the production of a mist of beryllium sulphate in concentrations between 100 and 1 mg. per cubic metre of air. A total of 11 species of animal were exposed, repeated daily 6-hour exposures being lethal to most species at concentrations of 50 mg. per cubic metre and above.

There were two types of reaction: an acute lethal type with few histological changes, and a delayed type in which surviving animals on further exposure appear at first to suffer little effect, but show increasingly severe changes on continued exposure. Details are given of changes in the body weight and blood, and of biochemical changes in urine and blood and histological changes in the lungs. Anaemia developed, together with changes in the blood lipoids and serum proteins indicative of deranged nitrogen metabolism, and alteration of arterial oxygen tension. The only cellular changes were in the lungs. In many species the pulmonary reaction to exposure resembled closely that seen in human acute beryllium poisoning. Photomicrographs are reproduced.

The authors conclude that inhalation of beryllium gives rise to a complex set of reactions and that these are due to the action of beryllium itself. Toxic effects occur at exposure and tissue concentrations far below those usually encountered in chemical toxicity.
A. Thelwall Jones

508. **Acute Inhalation Toxicity of Beryllium. II. The Enhancing Effect of the Inhalation of Hydrogen Fluoride Vapor on Beryllium Sulfate Poisoning in Animals**
H. E. STOKINGER, N. J. ASHENBURG, J. DEVOLDRE, J. K. SCOTT, and F. A. SMITH. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg. occup. Med.*] **1**, 398–410, April, 1950. 7 figs., 5 refs.

Potentially toxic dusts or vapours encountered in industry are frequently not single compounds but mixtures of various substances. An example occurs in the manufacture of beryllium, in which hydrogen fluoride and other fluorides are present. Experiments were made on rats to determine the enhancing effect of the inhalation of hydrogen fluoride vapour on beryllium poisoning. Experimental details are fully given. The authors conclude that inhalation of hydrogen fluoride vapour by rats at a concentration of 8 mg. per cubic metre enhanced twofold the toxicity of a soluble beryllium salt also inhaled by these rats. Inhalation of a beryllium salt as a mist at 9 mg. per cubic metre alternately with hydrogen fluoride increased the deposition of fluoride in tooth and bone to 1·3 times that from the inhalation of similar quantities of hydrogen fluoride vapour alone at 8 mg. per cubic metre. The mechanisms by which these effects occur are discussed. *A. Thelwall Jones*

509. **The Toxicity of Vapours of Organic Mercury Compounds (Ethyl Mercuric Phosphate and Ethyl Mercuric Chloride) under Acute and Chronic Conditions.** (О токсичности паров органических соединений ртути (этилмеркурфосфата и этилмеркурхлорида) при острых и хронических интоксикациях)
I. M. TRAKHTENBERG. Гигиена и Санитария [*Gigiena*] No. 6, 13–17, June 1950. 2 figs.

As preservatives of grain various chemical substances have been employed. Among these are the ethyl phosphate and ethyl chloride compounds of mercury.

Experiments were performed on white mice to determine the toxicity of these substances. Analyses were also made on collective farms and near or in grain stores. Some of these were performed in ventilated places or in the open, others under cover. It was found that mice died quickly if exposed to a concentration of 0·01 to 0·04 mg. per litre of air in the case of the ethyl mercury phosphate, and 0·03 to 0·04 mg. per litre in the case of ethyl mercury chloride.

Both acute and chronic mercury poisoning occurred, depending on the concentration of the fumes and the period of exposure. After 2 weeks or so the animals' behaviour changed; they became drowsy and refused food, and paralyses and tremor or clonic convulsions appeared later.

It is concluded that for use with grain even a trace of mercury should be avoided, because a concentration as low as 0·0001 mg. per litre is dangerous.

G. C. Pether

510. **Protective Clothing for Work with Mercury and its Cleansing.** (Спецодежда при работе со ртутью и очистка ее от последней)

K. V. Migaj. Гигиена и Санитария [*Gigiena*] No. 6, 17–20, June, 1950. 1 fig.

Experiments were made to determine the best type of clothing for use as a protective against mercury vapours or particles. Sundry textile materials were used; calico took up a smaller amount of mercury than any other material tested. The greatest adsorption occurred with army-uniform cloth. The tests were all made on the laboratory bench, and mercury in the material was estimated colorimetrically. For removal of mercury, washing was most effective if two changes of soft water were used, this technique being superior to any physical or chemical method tried. If exposed to the air, most material became nearly or completely free of mercury after 4 days.

G. C. Pether

511. **Arsine Poisoning. A Study of Thirteen Cases**

S. S. Pinto, S. J. Petronella, D. R. Johns, and M. F. Arnold. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg. occup. Med.*] **1**, 437–451, April, 1950. 16 refs.

Thirteen cases of arsine poisoning are described, and further details are given by colleagues of the authors in another paper in the same issue.

No reliable estimate of the arsine concentration in the air was possible, but the fumes were generated by moisture reacting with aluminium arsenide in metal dross. The usual symptoms of arsine poisoning were seen and these included abdominal cramps, nausea and vomiting, and the passage of a dark-red urine. The supernatant fluid from centrifuged blood samples was found to be dark red. The cases varied in severity and the first four patients to enter the hospital died.

The laboratory findings are given in detail and many interesting features are recorded. In the microscopical examination of urine no haemoglobin casts or cylindroids were found. There was no apparent correlation between the arsenic content of the urine and the amount of haemoglobin in the urine. Thus the urinary arsenic content is no measure of the degree of blood destruction. Initial leucocyte counts were made in 7 cases before any treatment was given, and these revealed a leucocytosis ranging from 13,000 to 29,000 per c.mm. The count returned to normal in all cases, but a further rise occurred on the fourth to sixth day after poisoning. Haematocrit readings showed evidence of rapid destruction of erythrocytes, haemoglobin accumulating in the plasma much faster than it could be removed or excreted. There was a rise in the non-protein nitrogen content of the blood, indicating that haemoglobinuria damages the excretory power of the kidneys. In all cases from the beginning serial electrocardiograms were taken, and changes were noted particularly in the T waves.

Only in one case was there a suggestion of jaundice. Treatment was mainly by transfusion of whole blood and there was no indication that such added blood was haemolysed. In the opinion of the authors, British anti-lewisite (BAL) had no influence on the course of the erythrocyte destruction produced by arsine. Whether BAL aids in preventing other disorders, such as peripheral nerve involvement, is as yet uncertain. Details are given of the necropsy evidence in 4 cases, death being due to sudden myocardial failure. The distribution of arsenic in the tissues is recorded, the figures agreeing in general with those in previous investigations.

A. Thelwall Jones

512. **Arsine Poisoning in the Smelting and Refining Industry**

K. M. Morse and A. N. Setterlind. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg. occup. Med.*] **2**, 148–169, Aug., 1950. 8 figs., 14 refs.

In January, 1949, 4 deaths from arsine poisoning occurred in Indiana, as a result of handling arsenic-bearing dross. The dross had been supplied by a firm in Illinois, and this led to an investigation of the smelting and refining plants in the latter State. During the progress of this investigation, 2 deaths occurred in an Illinois factory. The 2 men who died were engaged in ladling the dross formed in a large vessel of molten lead to which aluminium had been added to remove antimony and arsenic, which were present as impurities. The molten dross was placed in ingot moulds, which were then sprayed with water to facilitate cooling. Both men became ill 2 days after this work, and severe haemolytic anaemia and anuria developed. One man died after 7 days and the other after 3 weeks.

Detailed investigation into the chemical reactions of this dross, which consisted of lead (57·96%), aluminium (3·58%), antimony (10·95%), and arsenic (0·91%) revealed that the addition of water resulted in the evolution of hydrogen and arsine. High concentrations of arsine (300 p.p.m.) were found in the neighbourhood of the ingot moulds containing the dross if there was any moisture present.

Addition of water to mixtures of finely atomized lead and aluminium caused evolution of hydrogen and some oxygen. When arsenic was added to the mixture arsine was produced as well as hydrogen. The suggestion

is made that the difference in potential between the individual lead and aluminium particles created the conditions necessary for electrolysis, and the nascent hydrogen produced then reacted with the arsenic present to form arsine.

The form of the dross could be modified by adding sawdust as well as aluminium to the molten lead during purification; when the resulting "sawdust concentrate dross" was roasted in an oven for an hour at 1800° F. (982° C.) it became "stabilized" and would no longer produce arsine on contact with water.

W. K. S. Moore

513. **The Clinical Picture and Histopathology of Tetraethyl Lead Poisoning.** (К клинике и гистопатологии психотических состояний при отравлении тетраэтилсвинцом)

N. I. LASTOTCHKINA. Невропатология и Психиатрия [*Nevropat. Psikhiat.*] **19**, No. 3, 56–61, May–June, 1950. 5 figs.

The clinical features in 7 cases of tetraethyl lead poisoning were, on the whole, indicative of a subcortical and cerebellar disturbance. Status epilepticus was present in one of them, and another patient had a psychosis with no neurological signs. The psychopathological picture was dominated by persistent hallucinations and fear. One of the cases was fatal and the material was examined histologically. Foci of cell loss were diffusely distributed in the brain, being, however, more numerous in the subcortical centres and in the temporal and parietal lobes. Gliosis was not marked. The author stresses the importance of sleep and blood transfusion in the treatment of this condition. He found intramuscular administration of thiopentone particularly useful.

L. Crome

THERAPEUTICS

514. **Medical Applications of Microwave Diathermy: Laboratory and Clinical Studies**

F. H. KRUSEN. *Proceedings of the Royal Society of Medicine* [*Proc. R. Soc. Med.*] **43**, 641–658, Aug., 1950. 17 figs., 29 refs.

The development of the therapeutic use of various types of diathermy is reviewed and the author then describes his own association with the development of microwave diathermy as applied to medicine, the interruption of his experimental work during the war owing to shortage of equipment, and its recent resumption. Most of the experiments described were carried out with a small portable experimental type of microwave generator, containing an air-cooled multicavity magnetron with a maximum output of 125 watts, operating on a frequency of about 2,450 megacycles per second. Microwave diathermy has the great advantage over other forms of tissue heating that the waves behave like light waves and can therefore be focused by means of a suitable type of metal lens and directed to any part at will. The author and his colleagues have also concluded that absorption of microwave energy by the tissues is greater than that of energy produced by high frequency radiations of longer wave-lengths, a greater rise of temperature in muscle at a depth of 3 cm. being obtained with microwave than with short-wave diathermy for the same degree of heating of the subcutaneous tissue. Thus adequate heating of muscle, and at the same time a marked increase in blood flow, can be produced almost without systemic heating. When burns were intentionally produced in anaesthetized dogs it was noticed that the maximum damage was present in regions where bone was underlying the irradiated tissue and in regions of localized accumulation of tissue fluids. It is therefore suggested that in the presence of oedema, effusions, and abscesses, and in the case of such organs as the eye, gall-bladder, and urinary bladder, microwave irradiation may lead to overheating unless the dosage is carefully controlled. The reason for this phenomenon is the high absorption of microwaves by fluid.

To reduce the effects of reflection at the surface of the skin, and to make the transfer of energy from air to tissues more effective, an impedance-matching device or "transformer" has been developed and has proved satisfactory. More work is being done in this connexion, and with further knowledge of the dielectric constant of various tissues at various microwave frequencies a still more flexible method of heating particular types of tissues should be available. The author concludes on a note of warning, pointing out that more experimental work is still required before microwave diathermy can be used effectively as a therapeutic agent.

M. H. L. Desmarais

515. **Physiologic Mechanisms of Intra-arterial Transfusion**

P. G. JONES, J. H. DAVIS, C. A. HUBAY, and W. D. HOLDEN. *Surgery* [*Surgery*] **27**, 189–197, Feb., 1950. 5 figs., 9 refs.

In haemorrhagic shock intra-arterial transfusion is relatively much more effective than intravenous transfusion. In a dog exsanguinated to the point of cardiac and respiratory arrest, intra-arterial transfusion quickly raised the intra-aortic pressure and restored the coronary circulation. The heart-beat then started again and strengthened rapidly; this further raised the intra-aortic pressure. Reflex peripheral vasodilatation followed, with consequent rapid flow through the capillary networks throughout the body, including those in the brain and kidney. Respiration and renal function were re-established.

The perfusion of normal saline into an artery produced similar dramatic recovery from exsanguination, but the recovery was transient and severe shock quickly recurred. This did not happen after the intra-arterial transfusion of whole blood unless there was continued, and perhaps concealed, haemorrhage. *Francis F. Rundle*

516. **Further Studies of Agglutination and Inhibition in the Le^a-Le^b System**

O. J. BRENDEMOEN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 335–341, Sept., 1950. 11 refs.

Radiology

517. **Results of Physical Measurements in a Case of Occupational Radium Poisoning with a Fatal Outcome.** (Untersuchungen zum Problem der Radiumvergiftung. V. Ergebnisse physikalischer Messungen an einem Fall von gewerblicher Radiumvergiftung mit tödlichem Ausgang)
H. MUTH and H. H. ROTH. *Strahlentherapie* [*Strahlentherapie*] **80**, 271–380, 1949. 12 refs.

While working with radium and mesothorium, a chemist acquired radium poisoning which ended fatally. In the years 1932–1937 he was examined at intervals; results of all investigations including blood count were normal. In the autumn of 1940 the first clinical changes were observed, rales appearing over the apices of the lungs, but other findings were normal. At the beginning of 1943 a rapid change for the worse was noted; the haemoglobin content was 17%, erythrocyte count 800,000 per c.mm., and leucocyte count 1,800. Anti-anaemic therapy with numerous transfusions did not stop the progress of the disease. Radiographs of the lung showed, in the upper field, striae and patches of a bronchopneumonic character. Death occurred in 1944. Necropsy revealed aplastic anaemia, petechial haemorrhages in the pleurae, pericardium, and endocardium, marked pulmonary fibrosis, and pale bone marrow. The radioactivity of different parts of the body was determined with sensitive counters, and the whole content of radioactive substance was estimated at about 3·5 μg., the bone marrow being about 500 times more radioactive than the heart muscle. The patient's clothes showed marked radioactivity. The combination of aplastic anaemia and pulmonary fibrosis is unusual. Since 1937 irradiation ulcers had also been present in the skin of the hands. *Y. T. Seuderling (Excerpta Medica)*

RADIOTHERAPY

518. **Beryllium Window Radiations for Superficial Therapy**
A. C. CIPOLLARO. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **62**, 214–221, Aug., 1950. 3 figs., 2 refs.

A new type of *x*-ray apparatus for use in dermatological practice is described which emits extremely soft radiation (softer than Grenz rays; half-value layer (H.V.L.) 0·36 mm. of aluminium) at a high intensity owing to the use of a beryllium window fused in the glass of the tube. Such a window has an absorption corresponding to about 0·1 mm. of aluminium, and when the tube is operated at 30 kV and 1 ma., the H.V.L. of the rays emitted is 0·06 mm. of aluminium and the output is 268 r per minute at a focus–skin distance of 15 cm. Under these conditions the apparatus is suitable for the treatment of lesions at a depth of 2 to 3 mm., because 85% of the radiation is absorbed in the first 3 mm. of tissue. More penetrating rays can be produced by varying the added filter, the kilovoltage, or the focus–skin distance. *Basil A. Stoll*

519. **Absorption of Roentgen Rays with Use of a Beryllium Window Tube**
M. F. ENGMAN, E. P. WEBER, and W. G. ELLE. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **62**, 222–229, Aug., 1950. 2 figs., 9 refs.

The physical characters of the rays emitted by a beryllium-window *x*-ray tube have been investigated by the authors, using a black nylon thimble chamber. Polystyrene (density 1·05 to 1·08) was used as a phantom for measurement of depth dose. Measurements in air showed a falling-off definitely greater than would be expected by the inverse square law, suggesting some degree of air absorption. Back-scatter values for such soft radiations (if no filter is used) are so low as to be negligible and are independent of field size. The advantage of limiting radiation to the first 4 mm. of the skin is stressed, in that the blood vessels below this level are relatively unaffected and thus no atrophy of the skin results. *Basil A. Stoll*

520. **Results of Radiation Treatment of Pituitary Tumours.** (Ergebnisse der Strahlenbehandlung von Hypophysentumoren)
D. NITTINGER. *Strahlentherapie* [*Strahlentherapie*] **82**, 367–378, 1950. 17 refs.

An account is given of radiation treatment of 31 cases of pituitary tumour. Without histological confirmation, 8 appeared to be cases of acromegaly, 2 of Cushing's syndrome, and 21 of chromophobe tumour. The author uses 7 to 9 fields, giving 300 r to one or two fields daily to a total combined dose of 15,000 to 18,000 r. [No details are given of the all-important tumour dose or other technical factors.] Of 8 patients with acromegaly, 5 were alive after 5 to 8 years; headache and obesity were relieved, and expansion of the sella was arrested. Both of the patients with Cushing's syndrome improved. Cystic lesions responded far less than did tumours.

The higher dose range was associated with fewer recurrences than the lower, and a single high-dose course was better than repeated low-dose courses. If high dosage fails, operation should be considered, but an interval of 3 months should elapse to allow subsidence of the reaction.

In general, 15 cases improved without recurrence, 12 of these patients surviving for 5 to 13 years; 6 did well for 5 to 15 years after a second course; 4 died of their tumour after improvement, 4 showed no effect of the radiation, and 2 died of intercurrent disease after improvement.
J. Walter

521. **Radio-iridium Teletherapy.** [In English]
H. F. FREUNDLICH, J. L. HAYBITTLE, and R. S. QUICK. *Acta Radiologica* [*Acta radiol., Stockh.*] **34**, 115–134, July–Aug., 1950. 14 figs., 30 refs.

Radio-iridium emits γ rays with a mean energy of 400 kV, so that there is little difference in the energy absorbed by tissues of different density; thus irradiation with these γ rays has the same advantages as with those from radium. Protection, however, is much easier, for lead is $2\frac{1}{2}$ times more efficient in absorbing 400-kV radiations than in absorbing radium γ rays. Radio-iridium was therefore chosen as a suitable material for use in teletherapy, and the authors describe a unit designed for that purpose, with a 10-curie source. The treatment head, which is constructed of lead, is only 12·5 cm. in diameter; by mounting the source eccentrically in a lead cylinder, which can be rotated to an "on" or "off" position, adequate protection is obtained without removing the source from the head between treatments. At a focus–skin distance of 8 cm. the dose is 10 r per minute at the face of the applicator. As radio-iridium has a half-life of only 70 days, two identical sources are used, one being reactivated in the Harwell pile while the other is in use. The depth dose and the shape of the isodose curves are similar to those obtained with teleradium units.

Frank Batley

522. **Radium Treatment of Papillomatosis of the Male Urethra.** (Zur Radiumbehandlung der Papillomatosis der männlichen Harnröhre)
E. HEINKE. *Strahlentherapie* [*Strahlentherapie*] **82**, 383–386, 1950. 6 figs., 12 refs.

A case of multiple urethral papillomatosis in a man of 36, due to gonorrhoea, is described, and endoscopic findings are illustrated. Treatment was by intracavitary radium, 11 containers of 2 mg. each being applied in a catheter; filtration of iridio-platinum plus 1 mm. brass was used. Three doses of 150 r were given at 3-day intervals, followed a month later by 550 r similarly; the total dose was thus 1,000 r. Reactions were minimal and definite resolution was visible endoscopically 4 weeks later. A year later there was no trace of the lesions. To date, after 2 years, there have been no recurrences or complications, such as stricture. *J. Walter*

RADIODIAGNOSIS

523. **Osteoporosis and Diffuse Plasmacytosis.** (Osteoporose und diffuse Plasmozytose)
E. MORVAY. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **73**, 349–357, July, 1950. 9 figs., 7 refs.

All spontaneous fractures indicate a serious, though perhaps latent, underlying disease (except for fatigue fractures). Bone softening associated with demineralization and formation of osteoid tissue causes deformities but not fractures. Pathological fractures are mainly caused by osteoporosis, with characteristic thin bone which is neither decalcified nor deformed. This includes the following conditions: (1) senile osteoporosis; (2) osteoporosis as a result of "aggressive growth" of osteogenic or other tissue; (3) endocrine osteoporosis; (4) disuse osteoporosis in nervous diseases; (5) osteoporosis due to inflammatory processes, which, however, rarely causes spontaneous fracture.

The second group provides the majority of spontaneous fractures. Of the primary osteogenic tumours reticuloma shows a special tendency to cause spontaneous fractures. Apitz emphasizes that different forms of plasmacytoma represent different stages of a single disease. The sufferer from plasmacytoma often does not seek medical advise until spontaneous fracture occurs. The initial stage frequently cannot be seen in the radiograph. The next stage, which is evident in the radiograph, is usually that of solitary plasmacytoma. The most characteristic stage is that of multiple plasmacytoma, when multiple foci of invasion are evident. Symptoms are not conspicuous. Calcium balance is not affected. Most frequently, fractures occur in the spine and are associated with kyphosis. Ribs are also frequently affected. The disease then becomes generalized and all bones are affected. Calcium deposits appear in the kidneys and lungs. Pathologically, this is a benign process, though not really benign from the clinical point of view; the process may, however, undergo malignant degeneration (reticulosarcoma, Ewing's tumour, lymphosarcoma, myelosarcoma).

Radiographs show no tumour, no osteolytic destruction, no bone expansion, and no periosteal reaction. There are also no appearances suggesting a large bone cyst. Radiologically, there is widespread osteoporosis with bone trabeculae wide apart. In diagnosis, senile osteoporosis may be excluded, as patients are usually middle-aged. The tendency to spontaneous fracture is much greater than in senile osteoporosis. Although the spine has been regarded as the site of predilection of plasmacytoma, the author is of the opinion that flat bones are more frequently affected. Appearances in the spine are not characteristic, but those in the pelvis are much more distinctive; small, round, pea-like foci of osteoporosis are surrounded by sclerotic bone. In flat bones like the scapula, appearances are those of small multiple cysts. The clavicle breaks very easily. Osteoporosis in ribs extends into the calcified cartilage. In long bones some periosteal reaction is present, and in the lower limbs osteoporosis is followed by deformity, as in osteomalacia. Callus production is often affected and re-fracture is common. The author has seen no characteristic changes in the skull but, if affected, the bones show ill-defined areas of osteoporosis. *L. G. Capra*

524. **The Roentgenologic Manifestations of Acoustic Neuromas**
B. S. EPSTEIN. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 265–276, Aug., 1950. 4 figs., 30 refs.

A series of 21 cases of verified acoustic neuromata were studied. In plain radiographs the author found evidence of eighth-nerve tumour in only about 30% of his cases. Air studies were performed in 7 cases in which no abnormality had been seen in the plain films. Filling

of the lateral ventricles was complete in 5, all of which showed ventricular dilatation. In one case there was slight upward displacement of the ipsilateral temporal horn, and in one case of the occipital horn. The third ventricle was well seen in only 5 cases, in one of which there was deformity of the posterior part of its floor. Lateral displacement of the aqueduct was more evident than dorsal displacement. In 3 of 5 patients in whom the fourth ventricle filled it was displaced backwards, and in 2 its depth was diminished; rotation of the ventricle in the vertical plane was not observed. The ventriculographic features of acoustic neuromata reported in the literature are briefly summarized.

John Foley

525. **The Radiological Picture in Articular Changes of Late Congenital Syphilis.** (Il quadro radiologico nelle alterazioni articolari della sifilide congenita tardiva)
M. FACCINI. *Radiologia Medica* [*Radiolog. med., Torino*] **36**, 550–565, July, 1950. 8 figs., 27 refs.

Articular involvement in syphilis has been recognized for a very long time and its incidence is increasing, especially in the congenital form. This is most commonly a hydrarthrosis, often associated with Hutchinson's triad. The knee is the joint most commonly involved, followed in order of frequency by the elbow, shoulder, hip, and ankle.

Some authors distinguish only an osteo-arthritic and a pure arthritic form, but the present author prefers Hochsinger's classification of syphilitic joint lesions into two main types: (1) Without bone involvement: (*a*) simple hydrarthrosis; (*b*) hyperplastic synovitis. (2) With bone involvement: (*a*) white syphilitic tumour; (*b*) hydrarthrosis with productive bone changes (chronic deformative rheumatism of Virchow and Volkmann). Lesions of type (1) occur both in late congenital and in acquired syphilis, but more frequently in the congenital form, in which they may start more or less acutely and progress with exacerbations to eventual hyperplasia. The condition is frequently bilateral. Differentiation between the congenital and acquired forms is most difficult, the formerly-held belief that congenital syphilis of the joints is always unilateral and the acquired form commonly bilateral being erroneous. Radiographs show marked distension of the joint without involvement of the bone, although osseous changes will eventually be seen in the form of an increase of size of the epiphyses. Radiologically, differentiation from tuberculous hydrarthrosis is extremely difficult, if not impossible, the only distinguishing feature being the presence of some degree of bone atrophy in tuberculous lesions.

Of the second type of lesion, white syphilitic tumour is monarticular in the majority of cases. Bone involvement is constant, and involvement of the inguinal lymph nodes almost as constant, whereas the latter is absent in cases of white tuberculous tumour. The lesion may be synovial, osseous, or perisynovial and the radiological appearances depend on the location, extent, and morphology of the osseous lesion. In strictly articular (synovial) lesions, the appearances will be similar to those of the first form (abnormal opacity of the soft tissue of the joint) and not pathognomonic. The bony lesions are first seen in the femoral condyles and the patella, and originally consist of marginal erosions, the process progressing until there may be complete destruction of the patella. There is no evidence of perifocal reaction, although white syphilitic tumour is often associated with periostitis. Chronic syphilitic rheumatism, which is frequently polyarticular and symmetrical, may be associated with white pseudo-tumour, with normal articular appearances. This condition does not respond to specific treatment, in contrast to the true white syphilitic tumour which responds very well with radiological evidence of *restitutio ad integrum*.

In the differential diagnosis of syphilitic from tuberculous joint lesions four points must be emphasized: (1) Syphilis causes considerable destruction of the soft parts of the joints and comparatively little bone change. (2) Characteristic ulceration and scarring are present. (3) Periostitis is associated with the true syphilitic white tumour. (4) Articular new bone formation is present much sooner than in tuberculous lesions. It is also pointed out that typhoid and certain other fevers produce articular changes which can hardly be differentiated from those of syphilis. The radiological diagnosis of these lesions is very difficult and very often the radiologist can do no more than confirm the clinical and laboratory findings.

W. J. Czyzewski

526. **The Radiological Diagnosis and Radiotherapy of Osteoclastoma.** (Die Röntgendiagnostik und Strahlentherapie des Osteoklastoms)
E. MIGNOLI and U. COCCHI. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **73**, 391–411, Aug., 1950. 11 figs., bibliography.

The initial clinical manifestations of osteoclastoma are not characteristic and in some cases may be absent. The rate of evolution of the tumour from the earliest radiological manifestation to its full development varies considerably and the process may take weeks, months, or years. Ultimately 10% of all cases become malignant; in all probability these cases are atypical from their inception and the malignant degeneration is not caused by radiotherapy.

According to the frequency, degree, and extent of the atypical changes in the small cells, the tumour may be classified as " definitely benign ", " probably benign ", or " definitely malignant ", each type requiring different treatment. The most suitable treatment in cases in which atypical change is not too advanced is irradiation. Recurrences seem to be more frequent after combined operation and radiotherapy than after radiotherapy alone. Definitely malignant osteoclastomata are radioresistant, and in these cases operation is the treatment of choice. Although a clinical cure may follow radiotherapy immediately, the radiographic manifestations of the process of healing may extend over a period of years. Skin damage from radiotherapy is exceptional and is mainly met with after combined treatment. Continuous observation of all cases treated is essential in order to detect the earliest malignant changes and act accordingly. Recurrent tumours are just as radiosensitive as the primary.

A. Orley

527. **Intra-osseous Mucus-secreting and Cystic Epidermoid Carcinoma of the Jaw.** [In English]
A. SONESSON. *Acta Radiologica* [*Acta radiol., Stockh.*] **34**, 25–32, July–Aug., 1950. 5 figs., 5 refs.

528. **Problems of Angiocardiography**
R. H. MORGAN. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 189–195, Aug., 1950. 4 figs., 2 refs.

In view of the widespread routine performance of angiocardiography, the author draws attention to the danger of over-irradiation of the operator and also to the relatively high mortality among the patients examined. Measurements were made of the scattered radiation incident upon a radiologist standing at varying distances from the patient while a routine series of 8 films was made at peak voltage of 85 kV. The results obtained ranged from 10 milliroentgens at 1 foot (0·3 m.), down to 0·3 milliroentgens at 3·5 feet (1·07 m.) from the centre of the table.

In order to eliminate this hazard, the author has designed an automatic injector syringe, activated by a vacuum cylinder and piston which exert a pressure on the plunger of the syringe approximating to that normally exerted by the radiologist. This has been found to give most satisfactory results in practice.

In discussing the risk to the patient, the author describes 6 deaths resulting from angiocardiography. In 5 of these cases the patient had gross congenital cardiac defects, with central or peripheral pulmonary stenosis and cyanosis. In 2 cases death occurred after repetition of the injection for the purpose of obtaining a lateral view and it is suggested that there would be an appreciable lessening of the risk if a simultaneous series were taken in two planes, for which purpose an apparatus has been designed, and has just been completed, for the Johns Hopkins Hospital, Baltimore. *A. M..Rackow*

529. **Angiocardiography in Infants and Children. New Technic**
J. D. KEITH and J. D. MUNN. *Pediatrics* [*Pediatrics*] **6**, 20–32, July, 1950. 14 figs., 8 refs.

The authors describe in detail a special apparatus which they have devised for taking serial radiographs in infants at a rate of 4 per second. The use of this apparatus, combined with a very rapid injection of contrast medium into the femoral vein, has rendered possible the detailed study of congenital cardiac abnormalities in infancy. Since an angiocardiogram is usually of more value in cyanotic cases than in non-cyanotic, their study was directed chiefly towards demonstrating various right-to-left shunts. The radiological findings in a number of cases are recorded and radiographs reproduced showing the abnormalities which have been revealed by this method of investigation. These include not only the more frequent causes of cyanosis—tetralogy of Fallot, transposition of the great vessels, and dextrocardia—but also a number of interesting and rare anomalies.

In many cases angiocardiography may enable a clear-cut diagnosis to be made and in others it may provide additional information when the diagnosis is not in doubt. Rapid serial radiographs yield much more detailed and exact information than a single one, particularly in a cyanotic infant with a shunt from the right ventricle into the aorta, as in such cases the dye is often cleared very rapidly from the heart. It is emphasized that the chief usefulness of the technique described is in the neonatal period, when diagnosis is particularly difficult. The authors have examined 60 cases in this manner and have yet to find two alike. The dangers of the rapid intravenous injection of contrast media are appreciated, but only one fatality has been encountered. In general, infants tolerate the injection quite well and, in the experience of the authors, it is quite safe to investigate infants by this means in the first week or two of life, provided that not more than one injection of contrast medium is given on the same day.

Jas. M. Smellie

530. **A Simple Serialographic Technic for Cerebral Angiography**
L. S. ROSENBERG and J. R. SIMPSON. *Radiology* [*Radiology*] **54**, 869–874, June, 1950. 6 figs., 4 refs.

A simple and cheap method of cerebral angiography is described which permits the successive exposure of four 8×10-inch (20×25-cm.) films in 6 seconds. The cassettes are arranged in a Bucky tray, a lead sheet with an opening measuring 8×9 inches is placed on top of the radiography table, and the patient's head is positioned over this aperture. During the angiographic procedure the Bucky tray is shifted manually so that the four films come successively under the opening in the lead sheet and are exposed. The moving Bucky grid is used during each exposure. *F. M. Benton*

531. **Lung Cancer Operability. Angiocardiographic Study of Fifty-three Consecutive Proved Cases of Lung Cancer**
C. T. DOTTER, I. STEINBERG, and C. W. HOLMAN. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 222–28, Aug., 1950. 10 figs., 7 refs.

Angiocardiography has a field of usefulness in the assessment of operability of tumours of the lung. The authors have carried out angiocardiography in 53 consecutive cases in which cancer of the lung had been proved microscopically. From the findings, three categories of cases could be distinguished: (1) inoperable; (2) probably inoperable; and (3) not demonstrably inoperable. The criteria of inoperability adopted were as follows: (1) Partial or complete occlusion of the left pulmonary artery within 1·5 cm. of its origin, or of the right artery proximal to its bifurcation. (2) Partial or complete occlusion of the great veins in the mediastinum. (3) Demonstration of displacement or deformity of the unoccluded vessels within the mediastinum. (4) Demonstration of invasion of the pericardium in the form of local thickening in the absence of pleural disease in the vicinity.

Of the 53 patients examined, 22 were considered to show convincing evidence of inoperability. Eight of

these were explored and the findings confirmed; the others were not explored, but in most there was collateral proof of inoperability, though one case subsequently proved to be operable. Of 3 patients in whom the condition was deemed to be probably inoperable 2 subsequently underwent resection. Of 28 cases in which there was no angiocardiographic evidence of inoperability, exploration was carried out in 22 and resection performed in 12, the rest being inoperable. Of the 12 cases of resection, in 2 there proved afterwards to be mediastinal extension. The prognostic value of negative findings was therefore slight. The authors stress the fact that angiocardiography must be regarded only as a useful complement to other methods of assessment, and that no patient should be denied operation on the basis of the results of this examination alone.

A. M. Rackow

532. **The Differential Diagnosis of Unresolved Pneumonia and Bronchiogenic Carcinoma by Pulmonary Angiography**

P. G. KEIL and D. J. SCHISSEL. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **20**, 62–65, July, 1950. 5.figs., 8 refs.

Pulmonary arteriography was carried out on 26 patients with primary bronchial carcinoma, proved by histological examination, and 35 patients with resolving or unresolved pneumonia, 50 ml. of 70% diodone being injected into an antecubital vein percutaneously in 1½ seconds. Timing was started when 35 to 40 ml. had been injected and on the 2-second film the right heart and pulmonary tree were outlined. Decreased vascularity of the pulmonary parenchyma was demonstrated in 24 of the patients with carcinoma, and a relative increase of vascularity in the involved portion of the lung in 26 of the patients with pneumonia. It is suggested that decreased vascularity in pulmonary carcinoma may be due to (1) compression and obstruction of the arterial radicles by expanding and infiltrating neoplasm, (2) compensatory emphysema, and (3) necrosis of lung tissue. *Kenneth Marsh*

533. **Angiocardiography. The Prominent Pulmonary Artery Segment**

J. E. MILLER. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 214–221, Aug., 1950. 13 figs., 5 refs.

The author discusses the causes contributing to enlargement of the pulmonary artery shadow as seen forming part of the contour of the left border of the heart in the postero-anterior radiograph. He maintains that the bulge which is generally referred to as the shadow of the pulmonary conus is in fact that of the pulmonary trunk proper or of its left main branch.

From an analysis of findings in over 200 angiocardiographic examinations, he concludes that the main causes of prominence of the pulmonary artery segment are as follows: (1) Idiopathic dilatation, often discovered accidentally and without symptoms. (2) Pulmonary artery aneurysm. Six cases are included in the report. The differential diagnosis from carcinoma of the bronchus is frequently difficult, and should be settled by angiocardiography. (3) Patent ductus arteriosus. Enlargement of the pulmonary segment occurs in about 50% of cases. Angiocardiography reveals a localized bulge of the aorta in almost all cases of this condition. (4) Interatrial septal defect. A large pulmonary artery shadow is generally seen in this condition, the bulge being greatest in cases where mitral stenosis co-exists (Lutembacher's syndrome). In the author's experience interventricular defects do not cause pulmonary enlargement. (5) Eisenmenger's complex. The appearance of the pulmonary segment is variable here, the author having seen some cases of very considerable dilatation. The point is made that, since post-stenotic dilatation may occur, the fact that dilatation exists does not necessarily mean that the case is not one of Fallot's tetralogy. (6) Post-stenotic dilation of the pulmonary artery. Seven cases of dilatation associated with isolated pulmonary stenosis were seen. The heart is usually dilated to the right, and the author notes particularly that the pulmonary knob is usually high in position and almost obscures the aortic arch. *A. M. Rackow*

534. **Angiocardiography. Anatomoroentgenological Forms of the Transposition of the Great Vessels**

A. CASTELLANOS, R. PEREIRAS, and O. GARCIA. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 255–264, Aug., 1950. 7 figs., 7 refs.

The authors maintain that the anatomical arrangement of the transposed great vessels is not sufficiently constant to give a diagnostic contour to the cardiac shadow on plain radiographs, and state that the diagnosis can be made radiologically only by means of angiocardiography. They dispute the value of some of the diagnostic criteria laid down by Taussig, supporting their thesis by reference to 7 cases in which angiocardiography was performed by them, in 4 of which post-mortem examination was also possible (although in one of these the post-mortem examination consisted only of further angiocardiography).

Four types of transposition are recognized by the authors and illustrated by their cases: (1) The aorta arises from the right ventricle, passing to the right and in front of the pulmonary artery. Its subsequent course is normal. The heart is globular and the vascular pedicle not remarkable. (2) This type resembles the above, but the aorta arises almost at the midline and ascends slightly to the left. The cardiac outline is similar to that of type (1). (3) The aorta arises on the left side and its ascending portion forms part of the left heart contour. It then arches to the right and backwards over the left main bronchus, descending slightly to the left of the midline. The contour of the heart is grossly abnormal and the vascular pedicle is very wide. (4) The aorta passes from the left side upwards and to the right, crossing the mediastinum and arching over the right main bronchus. It may descend to the right of the mediastinum. In the angiocardiograph the common feature in all types is the immediate filling of the aortic arch from the right ventricle. The pulmonary artery is usually not visualized, and the left ventricle remains poorly opacified, if at all. *A. M. Rackow*

535. **Thoracic Aortography in the Diagnosis of Patent Ductus Arteriosus Botalli.** [In English]
B. BRODEN, G. JONSSON, and J. KARNELL. *Acta Radiologica* [*Acta radiol., Stockh.*] **34**, 65–81, July–Aug., 1950. 15 figs., 14 refs.

A brief description of the anatomy, pathophysiology, and clinical diagnosis of patent ductus arteriosus is given.

The authors explain why angiocardiography does not give a clear picture of the patent ductus; thoracic aortography must therefore be used. Details of the technique have been published in previous numbers of *Acta radiol., Stockh.* (1948, **29**, 181, and 1949, **32**, 498).

The procedure was carried out in 14 adults and 3 children. In 3 cases in which there was an atypical murmur the diagnosis could be established only with the aid of aortography. Out of the 14 adult cases 13 were operated upon, the diagnosis being confirmed.

F. M. Benton

536. **Tumours of the Heart.** (Über Herztumoren)
H. FRANKE. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **73**, 299–307, July, 1950. 14 figs., 13 refs.

Five cases of tumour of the heart are reported, with a description of symptoms, which vary considerably according to the site and extent of the tumour. In many cases diagnosis is very difficult, if not impossible. The most important complications are pressure effects.

Radiological examination reveals one direct and some indirect diagnostic signs. The direct one is a bulging of the vascular shadow, which is homogeneous, smooth, and non-pulsatile. Indirect signs are not characteristic. There is some enlargement of the affected cardiac chamber (radiological appearances often simulating those of mitral stenosis), calcification, or pericardial effusion. Many cases cannot be diagnosed, even with the help of several methods, mainly because the particular tumour has not altered the configuration of the heart. This is often the case with metastatic tumours.

In diagnosis the site, form, density, structure, contour, and influence on the surrounding organs (atelectasis) and on active and passive movements must be taken into account. All radiological means must be employed (screening, hard and soft radiography, kymography, and tomography). The author concludes with a list of the various sites of cardiac tumours and a brief outline of the differential diagnosis at each site.

L. G. Capra

537. **Radiological Visualization of the Coronary Arteries.** (Visualizacion radiologica de las arterias coronarias)
R. BUSTAMANTE, E. PÉREZ-STABLE, R. GUERRA, and B. MILANÉS. *Archivos del Instituto de Cardiología de México* [*Arch. Inst. cardiol. Méx.*] **20**, 350–356, June, 1950. 5 figs., 9 refs.

By retrograde catheterization of the brachial artery and introduction of the tip of the catheter to just about the aortic valve, the coronary arteries can be filled with an injection of 5 ml. of 70% " diodrast ". The closer the tip to the coronary arteries, the better the opacification. Filling was found to be easier in younger subjects [the authors offer no explanation of this, but it may well be due to the greater volume and efficiency of the coronary circulation in younger subjects]. No sign of coronary insufficiency was noted, though the arteries were well opacified. Illustrative radiographs are included.

R. A. Kemp Harper

538. **Cardiac Catheterization. V. Catheterization of the Left Heart in Man. Simultaneous Recording of Pressure and Intracavitary Electrocardiogram.** (El cateterismo intracardiaco. V. Cateterizacion de las cavidades izquierdas en el hombre. Registro simultaneo de presion y electrocardiograma intracavitarios)
R. LIMÓN LASON, V. RUBIO ALVAREZ, and F. BOUCHARD. *Archivos del Instituto de Cardiología de México* [*Arch. Inst. cardiol. Méx.*] **20**, 271–285, June, 1950. 9 figs., 6 refs.

The authors describe a method of retrograde catheterization of the aorta and left ventricle from the brachial artery. An ingenious catheter has been devised which enables simultaneous recording of the pressure in the aorta or left ventricle and of an intracardiac electrocardiographic tracing. The main hazard is accidental catheterization of a coronary artery, but this is guarded against by fluoroscopic control.

R. A. Kemp Harper

539 **Arteriography of the Aorta and its Branches by Means of the Polyethylene Catheter**
J. A. HELMSWORTH, J. MCGUIRE, and B. FELSON. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 196–213, Aug., 1950. 12 figs., 22 refs.

The authors have carried out angiocardiographic examination of 24 patients by catheterization of the brachial or femoral artery. The catheter used was made of polyethylene, a transparent plastic material, and its outside diameter was considerably smaller than the diameter of the lumen of the artery [a point of great importance]. Details of the technique are given.

By passing the catheter under fluoroscopic control down to the root of the aorta, an attempt to fill the coronary arteries was made in 6 cases. A partial filling was obtained in 2 cases, both patients being moribund and elderly; one of these died immediately after the injection. Satisfactory arteriograms of the thoracic aorta were made in 4 cases, revealing 2 aneurysms and a coarctation. In this last case the site and extent of the narrowing were well demonstrated. Retrograde abdominal aortography was undertaken in 4 cases, the catheter being passed upwards from the femoral artery in 3, and through the left brachial artery and down the whole length of the thoracic aorta in the fourth case. A satisfactory demonstration of intrinsic block of the abdominal aorta, with the establishment of a collateral circulation, was provided. The visualization of the innominate, subclavian, and common carotid arteries was successfully achieved by brachial catheterization. An operable aneurysm of the innominate was discovered and is described. In a further case, simultaneous filling of the right carotid and vertebral arteries yielded a diagnostic cerebral angiogram in a case of frontal menin-

gioma. Further cases described illustrate the exclusion of an anomalous right subclavian artery as a possible cause of oesophageal atresia in an infant, and the ease with which the diagnosis of arterio-venous aneurysm could be made in a case of swelling at the root of the neck.

In assessing the safety of the procedure, the authors remark that in this series no serious symptom could be attributed directly to the injection. The one patient who died was already moribund. In one case a convulsive attack was attributed to the passage of diodone to the cerebrum, and later practice has included compression of the carotids. No untoward effects occurred as a result of the opening of the artery, even in one case in which it was ligated after the catheter had been withdrawn. They conclude that the risk of the method must be weighed against the value of the diagnostic information procured. *A. M. Rackow*

540. **Radiological Symptomatology of Pericardial Adhesions.** (Zur Röntgensymptomatologie der Pericardverschwielung)
R. HAUBRICH and P. THURN. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **73**, 288–298, July, 1950. 7 figs., 21 refs.

Pericardial adhesions present a serious radiodiagnostic problem, unless the adhesions are calcified. Adhesions frequently cause displacement of the heart, and intrapericardial adhesions cause diminution of the retrocardiac space. Apparent posterior displacement of the heart when the patient is in the supine position is frequently caused by intrapericardial adhesions. Sometimes examination with barium swallow reveals pericardial adhesions of such degree that a traction diverticulum of the oesophagus has formed. Another sign suggestive of pericardial adhesions is pulsating traction on the diaphragm when the patient is holding his breath; this sign is not observed on ordinary screen examination, but is well seen in the kymogram. The traction is synchronous with systole. Movements of the mediastinal part of the "heart-bed", concomitant with the movements of the heart itself, are pathognomonic of constrictive pericarditis. Pericardial adhesions impair cardiac movements, even in cases in which no calcification of adhesions is present. This is especially true in cases in which adhesions have contracted with time. This contraction has a far-reaching effect on the auricles because their walls are comparatively thin. Ventricular adhesions are much more frequently encrusted with calcium salts than are those in the auricles. Because of this, contraction of ventricular adhesions is far less common. The differential diagnosis of pericardial calcification must be made from calcified cardiac thrombi, calcified cardiac aneurysm, and calcification of the cardiac valves or of coronary vessels. Calcification occurs mainly in the parts of the heart undergoing the least movement.

The authors describe at length the kymographic appearances in widespread calcification (*Panzerherz*). They emphasize the importance of changes in pulsation as observed in the kymographic picture. The function of the *Panzerherz* is impaired in one or other of its phases or in both of these. Factors influencing the extent of this impairment are: the thickness of adhesions, the degree of contraction of adhesions, the amount of calcification, the relations of the external adhesions, and the degree of damage to the myocardium. In cases of *Panzerherz* some parts of the cardiac outline show a somewhat exaggerated pulsation, which should be regarded as compensating for immobilization of other parts by calcification.

The authors describe a case of oesophageal stenosis due to traction by pericardial adhesions. *L. G. Capra*

541. **The Use of Gastric Mucin as a Barium Suspension Medium. A Preliminary Report**
G. H. ALEXANDER and R. E. ALEXANDER. *Radiology* [*Radiology*] **54**, 875–877, June, 1950. 2 figs.

Radiological study of the upper gastro-intestinal tract in which gastric mucin was used as a suspension medium for the barium meal showed no appreciable difference in the appearances from those obtained with the usual barium mixture, except that the small intestinal pattern showed greater delicacy of detail. Similarly, the use of mucin in barium-enema suspensions gave no significant improvement in outlining the colon.

For the meal, 2 g. of mucin was dissolved in water and this solution was used to prepare 250 ml. of barium mixture containing 125 g. of barium sulphate, while for the enema about 4 g. of mucin was added to the usual barium–water mixture. *F. M. Benton*

542. **Osseous Changes in Neural Leprosy. Radiological Findings.** [In English]
J. BARNETSON. *Acta Radiologica* [*Acta radiol., Stockh.*] **34**, 47–56, July–Aug., 1950. 33 figs., 9 refs.

Results are recorded of a survey of radiological changes in the bones of hands and feet of 107 adult lepers in South Africa. The principal changes were atrophy and disappearance of bone without productive changes, unless secondary infection had occurred. The degree of change depended on the duration of the disease, extent of nerve involvement, age of the patient, and history of trauma. The radiological changes in neural leprosy are not specific. *F. M. Benton*

543. **Osseous Changes in Neural Leprosy. Correlation between Histopathological and Radiological Findings.** [In English]
J. BARNETSON. *Acta Radiologica* [*Acta radiol., Stockh.*] **34**, 57–64, July–Aug., 1950. 11 figs., 8 refs.

The results are recorded of the study of radiological and histological changes in the bones of five lepers in South Africa.

Fraying of distal margins of the phalanges was associated with breaks in the continuity of cortical bone, the gaps being filled with connective tissue. When diffuse osteoporosis existed, cortical bone was narrowed and evidence of osteoclastic activity could usually be found. *F. M. Benton*

544. **Diaphragmatic Hernia of the Spleen.** (L'ernia diaframmatica della milza)
A. ROLLANDI. *Radiologia Medica* [*Radiol. med., Torino*] **36**, 642–653, Aug., 1950. 12 figs., 22 refs.

Pathology

545. **Cytological Observations after Intrapleural Nitrogen Mustard Therapy in 5 Cases of Carcinoma of the Pleura.** (Cytologische Beobachtungen nach intrapleuraler Losttherapie bei 5 Fallen von carcinomatöser Pleuritis)
H. J. STREICHER. *Archiv für klinische Chirurgie* [*Arch. klin. Chir.*] **266**, 55–73, 1950. 9 figs., 10 refs.

A cytological study was made of the pleural fluid of 5 patients suffering from carcinoma of the pleura who had been treated with injections of nitrogen mustard. In 4 cases the tumour was secondary to carcinoma of the breast, and in the fifth to a bronchial adenocarcinoma. The cytological results were very similar in all the first 4 cases, but were less obvious in the fifth case. In all cases the volume of the exudate and its specific gravity decreased progressively during treatment. There was a rapid decline in its cell content. The number of erythrocytes increased at first and later decreased. The leucocytes were represented at the end of the treatment almost entirely by lymphocytes. Endothelial cells increased in number in all 5 cases and showed phagocytic properties. Only a few isolated malignant cells appeared in the smears made at the end of the treatment. In these, nuclear and cytoplasmic changes became apparent after 5 days. The cytoplasm was intensely vacuolated, and there was a loose nuclear reticulum with many irregular-shaped granules. Hyperchromatosis of the nuclear membrane, as well as pyknosis and karyorrhexis, was common. Multinucleate cells were also observed. Similar cytological changes were seen in endothelial cells and blood leucocytes. *R. J. Ludford*

EXPERIMENTAL PATHOLOGY

546. **Pathology of Cerebrospinal-fluid Circulation and Experimental Hydrocephalus.** (Fisiopatologia della circolazione liquorale e idrocefalo sperimentale)
F. R. GRATTAROLA and G. KLUZER. *Acta Neurologica* [*Acta neurol., Napoli*] **5**, 385–401, July–Aug., 1950. 5 figs., 47 refs.

In cats the authors ligated the anterior choroidal artery on one side and then filled the anterior part of the third ventricle with " spongostan ", thus blocking both foramina of Monro. In those animals which survived this procedure hydrocephalus of both lateral ventricles developed; the ventricles were either equally large or the ventricle with interrupted blood supply was the larger. As this ventricle had been previously opened to carry out the ligation, it showed pathological changes such as ependymitis or oedema of the walls.

From these findings, the authors draw the conclusion that in pathological circumstances the cerebrospinal fluid may come from other sources than the choroid plexus. *F. K. Kessel*

547. **The Role of Immature Plasma Cells, Lymphoblasts, and Lymphocytes in the Formation of Antibodies, as Established in Tissue Culture Experiments**
F. J. KEUNING and L. B. VAN DER SLIKKE. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 167–182, Aug., 1950. 7 figs., 34 refs.

In experiments performed by the authors at the State University of Groningen, rabbits were given 3 injections of paratyphoid-B vaccine at weekly intervals. One to 4 days after the third injection they were bled to death and fragments of red and white splenic pulp dissected out, each weighing approximately 10 mg. These were divided equally, one portion being assayed for total antibody content immediately, and the other after 20 hours' tissue culture. A suspension was made of cells of other portions of the spleen and separated by slow centrifuging into two fractions, one containing the large immature cells and the other the small lymphocytes. Each fraction was then divided into two portions, which were treated as above. Moist smears were also made of red and white spleen pulp and were stained by the Unna–Pappenheim method as modified by Koch, the methyl green being highly specific for nuclear desoxyribose nucleic acid, and the pyronin indicating " cytoplasmic " ribose nucleic acid.

Antibody production is generally thought to be maximal 3 to 4 days after the last injection of vaccine and most of the material was examined at this stage. At this time the splenic Malpighian corpuscules showed active lymphopoiesis and the predominant cells were large and middle-sized immature lymphoid cells with strongly pyroninophilic nucleoli. Around these was a band of small lymphocytes. In the red pulp there were extensive aggregates of large pyroninophilic cells, (which, in 24-hour specimens, were only just beginning to develop). These cells appeared to be similar to the lymphoblasts of the white pulp.

Agglutinin production was always found in the tissue cultures of both white and red pulp. In explants removed 3 or 4 days after the last vaccine injection the new production of agglutinin was much greater in red than in white pulp. In explants removed 24 hours after the last injection the rate of production in the two tissues appeared about the same, that in the red pulp not having yet reached the high level found after 3 or 4 days. In the cell-suspension experiments, in which the tissue was always collected 3 or 4 days after the last injection, the vast majority of the cells were lymphocytes, which were classified as " large " or " small ", the other cells being disregarded. The large cells were of two types, the first being strongly pyroninophilic, with appearances suggesting protein synthesis. In control sections, these cells were found in the Malpighian corpuscles as well as in the characteristic cell aggregates in the red pulp, and have been variously named by different authors. The second type was the " immature plasma

cell " of Fragraeus, which was the main component of the characteristic cell aggregates of the red pulp on the third day. The small cells were mostly lymphocytes, without notable cytoplasmic pyroninophilia or true nucleoli. Hardly any mature plasma cells of the Marschalko type were present at this stage. The agglutinin titres of the fractions of suspensions depended on the total number of cells present rather than the proportion of large or small cells, though in tissue cultures the large-cell fraction produced a significantly higher proportion of agglutinin than the small-cell fractions. From this the authors conclude that the production of agglutinins is dependent on the presence of the large cells, and that although the smaller ones (lymphocytes) contain antibody, they cannot produce it nor multiply. These immature cells are active in protein synthesis, with a high content of cytoplasmic and nuclear ribose nucleic acid.

Peter Harvey

548. **The Effect of Radioactive Iodine Alone and in Combination with Methylthiouracil and Acetylaminofluorene upon Tumour Production in the Rat's Thyroid Gland**

I. DONIACH. *British Journal of Cancer* [*Brit. J. Cancer*] **4**, 223–234, June, 1950. 12 figs., 19 refs.

It has been shown that the prolonged administration of thiouracil to rats may give rise to goitres with the histological appearances of thyroid adenoma or carcinoma, and that 2-acetylaminofluorene (AAF) accentuates these changes.

In this paper from the British Postgraduate Medical School, London, the author describes the findings in 98 inbred rats given radioactive iodine (^{131}I), methylthiouracil, and AAF in various combinations. ^{131}I was administered alone in 2 doses of 16 μc. at 5½ months' interval, the thyroid uptake averaging 20% of these doses, and the rats were killed after an average period of 13 months from the initiation of treatment. The thyroid was reduced in weight in treated animals as compared with controls, but the incidence of adenomata was significantly increased. When ^{131}I was administered together with methylthiouracil, or with methylthiouracil and AAF, the increase in thyroid weight normally produced by these substances was lessened, but the incidence and size of adenomata were increased. One rat treated with ^{131}I and methylthiouracil, and one rat treated with ^{131}I, methylthiouracil, and AAF showed changes which were considered to indicate the development of carcinoma of the thyroid. The dosage of ^{131}I used in these experiments was of a similar order, in relation to the weight of the thyroid, to that used in the treatment of human thyrotoxicosis.

The author recognizes that the histological criteria of thyroid malignancy are subject to dispute, and quotes the finding of Gorbman (*Cancer Res.*, 1947, **7**, 746) that apparently malignant thyroid tumours with pulmonary deposits, induced in mice by treatment with thiouracil, regressed when the animals resumed a normal diet, and his suggestion that the metastases in these cases were of purely mechanical origin. It is suggested that ^{131}I has both a direct carcinogenic action on the thyroid cells and an indirect action by stimulating the production of thyrotrophic hormone. Prolonged administration of thyroxine, as in the treatment of nodular goitre, by inhibiting thyrotrophic-hormone formation may not only shrink the goitre, but also lessen the likelihood of mechanical production of thyroid metastases and of their survival.

G. Ansell

549. **Experimental Pulmonary Edema. IV. Pulmonary Edema Accompanying Trauma to the Brain**

E. M. MACKAY. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 695–697, Aug., 1950. 17 refs.

Fatal head injuries were produced in rats by application of a static force to one of two laterally placed wooden blocks gripping the head. The procedure was painless, resulting in instantaneous unconsciousness, and death within a few minutes. Pulmonary oedema occurred in almost all the animals. Its degree was assessed by inspection and from the ratio of lung weight to body weight.

The degree of oedema was unaffected by adrenalectomy carried out 3 hours before head injury. Deep narcosis, produced by pentobarbitone, ether, or chloral hydrate, protected against it. Oedema was also prevented by giving adrenergic blocking agents 30 minutes earlier.

M. Lubran

550. **Lesions of the Myocardium in Fat Embolism of the Lungs.** (О поражениях миокарда при жировой эмболии легких)

S. A. VINOGRADOV. Архив Патологии [*Arkhiv. Patol.*] **11**, No. 2, 47–60, March–April, 1950. 8 figs., 38 refs.

Fat embolism of the lungs was produced in rabbits by the intravenous injection of 1 to 1·5 ml. of olive oil. A condition analogous to acute cor pulmonale resulted, and degenerative lesions were found in the myocardium. The latter were situated chiefly in the right ventricle and included oedema, metachromatic staining of the ground substance, focal and diffuse degeneration of muscle fibres, and cellular infiltration and fibrosis. Apart from one case, no direct emboli were found in the coronary arteries, neither did any of the fat emboli reach the central nervous system.

L. Crome

551. **The Pathogenesis of Experimental Fat Embolism**

J. W. HARMAN and F. J. RAGAZ. *American Journal of Pathology* [*Amer. J. Path.*] **26**, 551–563, July, 1950. 4 figs., 12 refs.

Some of the factors involved in pulmonary embolism were studied. An extract of the perirenal fat of normal rabbits was injected intravenously into rabbits, the dose varying with body weight. The mortality rate was considerably elevated in animals suffering from tourniquet shock or dehydration. The administration of oxygen reduced the mortality rate from 50% in one group of controls to *nil*. Centrilobular hepatic necrosis, seen in animals with more severe degrees of pulmonary involvement, was prevented by oxygen treatment. No evidence of tolerance to repeated fat embolism was observed.

Brian E. Heard

552 (*a*). **Hepatic Necrosis Induced by Dietary Means. I. Structural Changes Occurring in the Liver during the Development of Necrosis**

M. R. ABELL, J. M. R. BEVERIDGE, and J. H. FISHER. *Archives of Pathology* [*Arch. Path.*] **50**, 1–22, July, 1950. 14 figs., 27 refs.

The authors, working at the University of Western Ontario, have studied the structural and biochemical changes which precede and accompany the development of massive hepatic necrosis in rats given a diet low in protein (7·2% yeast protein) and deficient in α-tocopherol. Altogether 121 rats were used, groups of 5 being examined at intervals from the 15th to the 92nd day. The general health of the animals was good until necrosis developed after 48 to 88 days (average 71). There were 5 control animals. At the end of 15 days' diet there was a marked loss of weight, and there was a definite decrease in the size of the hepatic lobules, with a loss of cellular cytoplasm. A progressive increase of fat in the centrilobular cells was noted in all animals killed before necrosis had developed, and glycogen granules were usually more prominent in portal areas.

Three types of necrotic lesion were seen. (1) Massive hepatic necrosis (11 deaths and 9 killed when moribund). The livers were enlarged, friable, and coarsely mottled owing to the presence of necrotic and haemorrhagic areas. All lobes were involved, but the left lobe was often more so. A few livers appeared merely to be very congested. The necrosis was extensive, but was less near or around the portal tracts than elsewhere. There was no evidence of regeneration, no increase in number of phagocytes, and no haemosiderin. (2) Submassive and recurrent submassive necrosis. Necrosis was present in 2 rats on the left side only; recurrent bouts of necrosis were observed in 14 animals. The livers were normal in size or slightly enlarged. Microscopically, the picture was similar in some areas to that of massive necrosis, but regeneration and scarring were present. (3) Post-necrotic scarring. The hepatic appearances were extremely variable; most livers were distorted by fibrous tissue, and nodules of regenerating tissue were sometimes found.

W. H. Horner Andrews

552 (*b*). **Hepatic Necrosis Induced by Dietary Means. II. Biochemical Changes Occurring in the Liver during the Development of Necrosis**

M. R. ABELL and J. M. R. BEVERIDGE. *Archives of Pathology* [*Arch. Path.*] **50**, 23–35, July, 1950. 10 figs., 11 refs.

The work reported in this paper is a continuation of the work described in the preceding paper (Abstract 552 (*a*)) on hepatic necrosis in rats due to dietary deficiency.

An initial decrease of wet liver weight occurred during the first 15 days on the diet. After this, little change took place until the advent of necrosis, which produced an increase in weight. The dry liver weight also decreased initially and was below normal in cases of submassive necrosis, but in those of massive necrosis it was increased. The water content of all non-necrotic livers was essentially constant, but was increased in necrosis. The glycogen content did not alter greatly in non-necrotic livers, but fell to extremely low levels in cases of necrosis, especially of the massive type. There was a progressive, but variable, increase in the total liver lipid content, necrotic and non-necrotic livers giving the same value. The neutral-fat and total fatty-acid contents ran parallel, but phospholipid values remained almost unchanged except in cases of massive necrosis, in which they were decreased. The total cholesterol content increased greatly in the pre-necrotic period, with a further elevation when necrosis supervened, due to an increase in the free cholesterol content, the cholesteryl-ester level being similar in necrotic and non-necrotic livers.

The results of analysis of post-necrotic livers were variable, presumably due in part to the varying degree of fibrosis. In general, however, the values obtained lay between those for pre-necrotic livers and livers showing massive necrosis. *W. H. Horner Andrews*

553. **Anaemia Induced Experimentally by Ligation of the Portal Vein.** (Anemia sperimentale da legatura della vena porta)

A. TORCIGIANI. *Rassegna di Fisiopatologia Clinica e Terapeutica* [*Rass. Fisiopat. clin. terapeut.*] **22**, 367–377, May, 1950. 16 refs.

In previously reported experiments (*Bull. Soc. ital. Biol. sper.*, 1949, **25**, 979) the author demonstrated that the repeated bleeding of dogs in which the portal vein had been tied resulted in a permanent anaemia. The experiments reported here show that a similar result can be obtained solely by tying the portal vein, and that the obstruction need not be complete. In 6 dogs the anaemia developed about 10 days after operation, the erythrocyte count and haemoglobin level showing a proportionate fall of at least one-third; there was no evidence of regeneration. The leucocyte count showed a similar fall, with a relative increase in polymorphonuclear cells, while the plasma protein content remained normal, though there was a slight increase in the plasma fibrinogen level. At necropsy 40 to 100 days later a well-marked collateral circulation had developed and the liver and spleen showed an atrophic fibrosis; there was a diminution of the erythrocyte precursors in the bone marrow.

Three main theories have been suggested by other workers to explain similar, but not identical, findings after various types of obstruction to the portal system: (1) deficiency of gastric haemopoietin; (2) failure of the liver to destroy an inhibiting substance produced by the spleen; and (3) inability of the digestive tract to utilize iron and other dietary factors. Interpretation of the present results by means of any of these theories is difficult; but the permanent failure of erythropoiesis and lymphopoiesis, together with the maintenance of normal plasma protein values, suggests at least that liver function remains normal. *A. Paton*

554. **The Effect of Azaguanine on Mitosis in Normal and Neoplastic Tissues**

D. M. SHAPIRO, R. WEISS, and A. GELLHORN. *Cancer* [*Cancer*] **3**, 896–902, Sept., 1950. 11 figs., 5 refs.

555. **Lipotropic Effects of Liver Extract, Vitamin B_{12} and Choline**

H. M. McCormick and V. A. Drill. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 626–630, July, 1950. 8 refs.

In experiments carried out by the authors at Wayne University, Detroit, rats were fed on a high-fat diet containing 51% of lard, and controls on a diet containing 6% of lard, for periods of 30 to 150 days, certain supplements to the diet being injected subcutaneously. At the end of the period the fat content of each rat's liver was estimated both chemically and histologically. A lipotropic effect was exerted by the administration to the rats on a high-fat diet of a minimum of 1 ml. of crude liver extract (containing 1 *U.S.P.* unit of anti-anaemic principle per ml.) 3 times a week by injection, and the same dose was nearly as effective given by mouth. Administration of 2 mg. of choline 3 times a week, which is a larger dose of this substance than is contained in the above dose of crude liver extract, failed to exert a lipotropic action, as did a combination of 1 mg. of choline, 1 mg. of inositol, and 2 μg. of folic acid given three times weekly. Another experiment showed that the administration of crystalline vitamin B_{12}, with or without added choline, did not protect the liver from the effects of the high-fat diet.

Peter Harvey

556. **Pathologic Changes Induced in Guinea-pigs by Administration of Diets Deficient in the Anti-stiffness Factor**

P. N. Harris and R. M. Wulzen. *American Journal of Pathology* [*Amer. J. Path.*] **26**, 595–615, July, 1950. 16 figs., 40 refs.

Guinea-pigs (but not hamsters), when fed on a diet prepared from dried skimmed milk supplemented by all the known vitamins, develop calcifying necroses in voluntary, cardiac, and plain muscle tissue, and in blood vessels, liver, and kidney. In some lesions abscesses form.

[This paper with its photomicrographs of the remarkable arterial lesions should be inspected by all interested in vascular disease.] *D. M. Pryce*

557. **Interrelationships of Desoxycorticosterone, Cortisone and Vitamin C in the Genesis of Mesenchymal Lesions**

C. Schaffenburg, G. M. C. Masson, and A. C. Corcoran. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 358–365, June, 1950. 2 figs., 23 refs.

Degenerative and atrophic changes in the collagen of the heart and joints resembling those in rheumatic fever and rheumatoid arthritis have been induced experimentally by vitamin-C deficiency and by treatment with deoxycortone (desoxycorticosterone) acetate (DCA). The prevention and cure of such lesions by cortisone or adrenocorticotrophin (ACTH) led the authors to investigate the action of these substances in scurvy.

They gave 26 adult male guinea-pigs a scorbutic diet with 1% saline for drinking water. Six animals were given 5 mg. of DCA daily, 6 were given 5 mg. of cortisone daily, 6 were given 5 ml. of orange juice daily and served as normal controls, and 8 were kept as untreated scorbutic controls. Only animals in the first and last groups showed symptoms of scurvy: these appeared first and were generally more severe in the group receiving DCA. The body weight increased in the cortisone-treated and the normal control groups, but fell in the other two groups. Joint changes were absent from all but one of the animals receiving cortisone, but were severe in the DCA-treated and the untreated scorbutic controls. In all groups except the normal controls diffuse haemorrhages were present at necropsy, but they were less severe in the cortisone-treated group. Scurvy caused marked adrenal hypertrophy, which was completely prevented by treatment with cortisone and partly prevented by DCA. It is suggested that the scorbutic guinea-pig untreated or treated with DCA may be a valuable test animal for the assay of anti-arthritic compounds. *A. C. Crooke*

558. **Production of Rheumatic Subcutaneous Nodules**

S. Schwartz and O. Steinbrocker. *American Heart Journal* [*Amer. Heart J.*] **40**, 100–105, July, 1950. 1 fig., 6 refs.

In this paper from the Arthritis Clinic, Bellevue Hospital, New York, the literature concerning the production of "artificial" subcutaneous nodules in cases of rheumatic fever is reviewed and discussed and the authors describe their own attempts to produce nodules by three methods: (1) After infiltration of the area with procaine, 3 ml. of the patient's own blood was injected subcutaneously over the olecranon process, the patient rubbing the area for 10 minutes three times a day. (2) A 1% solution in M/400 hydrochloric acid of trypsin magnesium sulphate was passed through a Seitz filter and, within 48 hours, 1·0 ml. was injected over the olecranon. No friction was applied. (3) Fluid from the knee-joint in a case of moderately advanced (stage II) active rheumatic arthritis with naturally occurring subcutaneous nodules was tested for sterility and then (after a preliminary sensitivity test with 0·1 ml. of 1 in 100 dilution) 1·0 ml. of the sterile joint fluid was injected subcutaneously over the olecranon. Friction was applied as in experiment (1).

Eighteen of the subjects in experiment (1), 13 in experiment (2), and 8 in experiment (3) had rheumatoid arthritis, while 8 in experiment (1), 6 in experiment (2), and 4 in experiment (3) had rheumatic fever. Sixteen healthy subjects with no rheumatic history were used as controls. After 6 weeks' observation none of the subjects in experiments (2) or (3) developed nodules. In experiment (1) one of the subjects with active rheumatic carditis developed a doubtful area of induration which persisted for a fortnight, but showed a non-specific histological picture. *Peter Harvey*

559. **The Transplantation of Normal Tissues: with Special Reference to Auto- and Homo-transplants of Thyroid and Spleen in the Anterior Chamber of the Eye, and Subcutaneously, in Guinea-pigs**

M. F. A. Woodruff and H. G. Woodruff. *Philosophical Transactions of the Royal Society. B.* [*Philos. Trans., B.*] **234**, 559–582, Sept. 26, 1950. 38 figs., bibliography.

MORBID ANATOMY

560. **Circulatory Disturbances in the Brains of Immature Stillborn Infants.** (О нарушениях квовообращения в головном мозгу недоношенных новорожденных)
S. S. WAJL. Архив Патологии [*Arkhiv Patol.*] **11**, No. 2, 38–47, March–April, 1950. 7 figs., 6 refs.

Both naked-eye and microscopic haemorrhages are frequent findings in the brains of stillborn infants. The reticulin structure of blood vessels in such infants always deviates from the normal. Abnormalities may assume the following forms: (1) underdevelopment of the argyrophil structure; (2) lack of cohesion and fragmentation of the fibres; (3) thickening and deficiency in the reticulation of the fibres. The blood vessels themselves often contain miliary aneurysms and fusiform dilatations.
L. Crome

561. **Cysticercal Basal Leptomeningitis.** (Цистицеркозный базилярный лептоменингит)
F. L. LEJTES. Архив Патологии [*Arkhiv Patol.*] **11**, No. 2, 83–85, March–April, 1950. 2 figs., 10 refs.

A report is given of a case of cysticercosis of the brain with 2 living cysticerci in the frontal cortex and, in addition, a thickening of the basal meninges. Histological examination of the latter showed marked proliferation of fibrous tissue around remnants of cysticerci.
L. Crome

562. **Rheumatism-like Granulomata in the Myocardium of Tuberculous Patients.** (О ревматоидных гранулемах в миокарде туберкулезных больных)
N. N. GRITSMAN. Архив Патологии [*Arkhiv Patol.*] **11**, No. 2, 65–72, March–April, 1950. 4 figs., 28 refs.

In a series of 81 necropses granulomatous lesions resembling rheumatic nodules were found in 23 cases in patients dying from various forms of tuberculosis, coexistent rheumatism having, so far as possible, been excluded by reference to clinical history. Such lesions were not, however, identical with true Aschoff nodules. The author regards them as a manifestation of an allergic reaction, and does not agree with those Japanese workers who regard them as evidence of the tuberculous aetiology of rheumatism.
L. Crome

563. **Changes in Skeletal Muscle in Acute Rheumatism.** (Изменения скелетной мускулатуры при истинном ревматизме)
E. J. GERTSENBERG and R. L. SKOMAROVSKAJA. Архив Патологии [*Arkhiv Patol.*] **11**, No. 2, 18–23, March–April, 1950. 5 figs., 8 refs.

Lesions of skeletal muscle in acute rheumatism vary in accordance with the pathological changes in the heart. In cases with pure valvular defect the muscular lesions consist of swelling and atrophy of muscle fibres, loss of striation, clumping and multiplication of sarcolemmal nuclei, and occasional waxy degeneration of the fibres. The above changes are degenerative and non-specific in character. In cases with recurrent rheumatic endocarditis there are, in addition, more specific features. The blood vessels are surrounded by cellular infiltrate. The muscle fibres may be fragmented and separated by serous exudate. The vascular endothelium is swollen. Fibrinoid necrosis of the vessel wall may be present. Miliary foci of muscle necrosis are also sometimes found. Granulomatous lesions consisting of lymphocytes, histiocytes, and large mononuclear cells may be found as well as patches of fibrosis.
L. Crome

564. **Rheumatic Lesions of the Lungs and the Skin.** (Ревматическое поражение легких и кожи)
A. G. BEGLARJAN. Архив Патологии [*Arkhiv Patol.*] **11**, No. 2, 85–89, March–April, 1950. 3 figs., 10 refs.

A case of rheumatic heart disease is recorded with lesions in the lungs and a rheumatic purpura of the skin. Histological study of these lesions revealed fibrinoid necrosis of blood vessels, with a polymorphonuclear infiltration of all vascular coats. The alveoli of the lungs contained fibrinous masses.
L. Crome

565. **The Morbid Anatomy of Silicosis.** (Патологическая анатомия силикоза)
F. I. POZHARISKIJ, M. S. TOLGSKAJA, and A. P. SHILOVA. Архив Патологии [*Arkhiv Patol.*] **11**, No. 2, 23–32, March–April, 1950. 6 figs., 18 refs.

The authors record their findings in a pathological and clinical study of 15 cases of silicosis. Tuberculosis also was present in 7 cases. There was no correlation between the severity of the clinical condition and the number of silicotic nodules. The symptoms were, however, related to the degree of associated fibrosis of the lung.
L. Crome

566. **Pulmonary Changes due to Cardiac Disease with Special Reference to Haemosiderosis**
A. C. LENDRUM, L. D. W. SCOTT, and S. D. S. PARK. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **19**, 249–262, July, 1950. 18 figs., 53 refs.

Haemosiderotic foci of varying extent were found in the lungs of patients with mitral stenosis only when there was hypertrophy of the right ventricle, foci being strikingly absent when there was concomitant tricuspid stenosis. In a proportion of cases this pulmonary haemosiderosis can be detected many years before death and is sometimes present in symptomless cases.

The pigment-laden histiocytes are found packing groups of adjacent alveoli in relation to respiratory bronchioles and alveolar ducts; this grouping points to mechanical rupture of the broncho-pulmonary anastomotic channels due to the pulmonary hypertension. Similar foci are found in cases of episodic left ventricular failure. In cases of rapidly-fatal left ventricular failure (essential hypertension, nephritis of short duration, acute rheumatic carditis) the fibrinous exudate was seen on close inspection only in alveolar ducts and their related alveoli, suggesting that the broncho-pulmonary anastomotic plexus extends farther down than has previously been suspected. Exudation of fibrin presumably occurs because the right ventricular preponderance is of shorter duration than in mitral stenosis. In some cases of severe rheumatic carditis fibrinous plugging of vessels in the alveolar-duct wall was also found.
W. S. Killpack

567. **Xanthomas of the Choroid Plexus in Man**
A. WOLF, D. COWEN, and S. GRAHAM. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath. exp. Neurol.*] **9**, 286–297, July, 1950. 8 figs., 17 refs.

Twenty examples of choroid-plexus xanthoma were encountered in 1,181 consecutive necropsies. They were invariably found in the glomus of the choroid plexus of the lateral ventricles and were in four instances solitary and in the remainder multiple, with as many as six individual lesions in a glomus. Varying in size from a pin-point to 8 mm. in diameter, and in colour from dull yellow to bright or orange yellow, they were incidental findings in middle-aged or elderly persons who had died from other causes; only one of the 20 suffered from diabetes.

Histologically, the xanthomata are composed of large lipoid-laden mononuclear cells with small deeply-staining eccentric nuclei; these arise from the arachnoid cells in the stroma of the choroid plexus, for transitions can be made out. That a phagocytic capacity should be retained by the isolated arachnoid cells of the choroid papillae is consistent with our knowledge that phagocytes in the subarachnoid space arise from arachnoid cells.

Cholesteatomata of the choroid plexus were first described in the horse by Fürstenberg (1851), but human cases were not recognized with certainty until Blumer's report (1900) of one which measured 22 mm. in its maximal diameter. Cushing and Eisenhardt (1938) proved that bilateral specimens in the Hunterian Museum, described as " scrofulous tubercles " by Matthew Baille (1812), were in point of fact xanthomata.

W. H. McMenemey

568. **Neurilemmoblastosis. The Influence of Intrinsic Factors in Disease when Development of the Body is Abnormal**
K. INGLIS. *American Journal of Pathology* [*Amer. J. Path.*] **26**, 521–549, July, 1950. 24 figs., 9 refs.

Four cases are described in which there were miscellaneous malformations together with tumours.

The first patient, a woman of 41 years, with emphysema and right heart failure, died from pneumothorax. She had had adenoma sebaceum since childhood, and peculiar nodules were present in the kidneys, uterus, liver, and lung. The kidneys also contained a few cysts, and the condition present in the lung may have been congenital cystic disease. She also had a duct papilloma of the breast.

In a boy of 4 months tuberous sclerosis, cystic kidneys, and pale nodules in the heart (congenital glycogenic rhabdomyomatosis) were found. The third patient, a woman of 56, had an encapsuled tumour in a kidney which was excised. The fourth, a woman of 32 with polycystic lungs, died from pneumothorax.

The tumours in the kidney and elsewhere were probably fibrolipomatous or fibromyomatous, but the author thinks that the spindle cells here and in foci in lungs and lymph nodes were neurilemmatous. From this he goes on to suggest that all the tumours and malformations (including the duct papilloma) resulted from the influence of " neurilemmal intrinsic " or " basic intrinsic " factors. [Not all the cases were adequately examined and the hypothesis seems insecurely based.]

D. M. Pryce

569. **Amyloid and Myeloma**
D. C. DAHLIN and M. B. DOCKERTY. *American Journal of Pathology* [*Amer. J. Path.*] **26**, 581–593, July, 1950.

Amyloid material, giving characteristic reactions with methyl violet, methyl green, van Gieson, and Congo red stains, was found in 14 out of 66 personally-studied cases of plasma-cell tumour. In 2 of the cases intracytoplasmic inclusions, staining weakly for amyloid, were present in the larger tumour cells. It is suggested that the presence of amyloid within a tumour of debatable nature is almost diagnostic of myeloma; it is also thought that plasma cells produce amyloid or some precursor of the latter. Necropsy findings in 2 cases of myelomatosis are also described; in one there were widespread amyloid deposits, in the other local deposits only.

A. Wynn Williams

570. **The Morbid Anatomy of the Mesenteric Lymph Nodes in Infants Dying of Acute Diarrhoea.** (Estudio anatomo-patologico de los ganglios mesentericos de los niños muertos de diarreas agudas)
A. CASTELLANOS and F. SALAS. *Archivos de Medicina Infantil* [*Arch. Med. infant.*] **19**, 63–95, April–May–June, 1950. 6 figs., 21 refs.

The authors studied the morbid anatomy of the mesenteric lymph nodes in 43 infants dying of acute diarrhoea in the Havana Municipal Hospital for Children. All cases showed the histological changes of acute or subacute adenitis. An eosinophilic reaction was noted in some cases, but the predominating lesion in the series was a great enlargement of the lymphoid follicles, large numbers of clear reticular cells being found in their central zones. This central follicular reaction occurred mostly in those children who had had symptoms for more than 7 days. The histological findings are described in detail, and mention is made of the bacteriology of the various infections and the therapeutic measures employed.

René Méndez

571. **Changes in the Muscularis Mucosae in Chronic Gastritis.** (Modificazioni della muscularis mucosae nella gastrite cronica)
P. GULLINO and E. FOGLIATI. *Archivio per le Scienze Mediche* [*Arch. Sci. med.*] **89**, 367–397, May, 1950. 17 figs., 11 refs.

In a study of 100 cases of chronic gastritis the authors found characteristic hypertrophic changes in the muscularis mucosae, particularly of the antral region. Not only was this muscle layer increased in thickness and the muscle cells increased in size, but prolongations extended up into the mucosa to a higher level than normal. It was considered that some sclerotic process might hinder the normal mucosal movement, calling for additional action on the part of the muscularis mucosae and producing a condition of work hypertrophy.

In order to test this hypothesis an experiment was undertaken on dogs. In a group of animals treated with

histamine, and later with cincophen, they failed to find any similar lesions, but in another group changes identical with those found in the human cases were found when pieces of celluloid were inserted into the gastric wall and left *in situ* for 50 days. The celluloid was placed in the submucosa and presumably hindered normal mucosal movement. The authors consider that their hypothesis was further supported by a case in which similar changes were found in relation to a small myoma of the gastric wall found accidentally at a routine post-mortem examination. *G. J. Cunningham*

572. **The Intercellular Substance of the Connective Tissue in Myxedema. A Morphological and Histochemical Study**
G. ASBOE-HANSEN. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **15**, 25–32, July, 1950. 1 fig., 28 refs.

The amount of intercellular and interfibrillar substance in cutaneous connective tissue is governed by thyroid function, perhaps by way of variations in hyaluronidase concentration. In myxoedema there is an excess of metachromatic intercellular substance of an acid polysaccharide nature (consisting wholly or partly of hyaluronic acid), which may be kept at a comparatively low level by the administration of thyroid. " Normal " skin from a thyrotoxic patient shows no metachromasia. The injection by the author of hyaluronidase into areas of typical localized myxoedema reduced the amount of metachromatic intercellular substance present, and made demonstration of its acid polysaccharide character more difficult. Numerous large mast cells with varying degrees of granulation are to be found throughout myxoedematous tissue, and histological evidence is submitted to support the theory that hyaluronic acid is secreted by such cells. *James Marshall*

573. **Malignant Testicular Tumours, Particularly Chorionepithelioma, and the Possibility of Spontaneous Cure of Primary Testicular Teratoid, with a Note on Diabetes Insipidus.** (Über die bösartigen Hodengewächse, insbesondere das Chorionepitheliom und die Möglichkeit der Spontanheilung des primären Hodenteratoids, mit einem Beitrag zur Frage des Diabetes insipidus)
F. ROTH. *Zeitschrift für Krebsforschung* [*Z. Krebsforsch.*] **57**, 21–69, 1950. 17 figs., bibliography.

From a study of 9 cases of testicular tumour the author concludes that seminoma is a " teratoid " tumour, and that all malignant tumours of the testis are related " teratoblastomata ". Chorionepitheliomatous tissue is more often present in malignant teratomata than has been supposed. A case of rupture of the spleen due to metastases of a testicular chorionepithelioma in a man of 42, and another of disseminated chorionepithelioma with retrogression of the primary testicular tumour (like those reported by Prym, Michel, and others) and accompanied by gynaecomastia, are described and the hormonal effects of testicular tumours are reviewed and discussed. In the latter case the patient had also had diabetes insipidus, which necropsy showed to be due to a coincidental chronic inflammatory lesion of the pituitary. *R. A. Willis*

CLINICAL PATHOLOGY

574. **The Position of the Oxygen Dissociation Curve of the Blood in Normal Children and Adults**
M. MORSE, D. E. CASSELS, and M. HOLDER. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1091–1097, Aug., 1950. 3 figs., 47 refs.

The authors confirmed the well-known fact that the oxygen dissociation curve of the newborn infant lies to the left, and that of the child to the right, of the dissociation curve of the adult. There is an exhaustive discussion of possible explanations taken from the literature, but no conclusion is reached. *P. Mestitz*

575. **The Position of the Oxygen Dissociation Curve of the Blood in Cyanotic Congenital Heart Disease**
M. MORSE, D. E. CASSELS, and M. HOLDER. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1098–1103, Aug., 1950. 3 figs., 12 refs.

In a study of 29 patients (4 adults and 25 children) at the Chicago University Clinic, the authors found that the oxygen dissociation curves were displaced to the right of normal. This shift was greatest in those patients who had pulmonary stenosis; in 4 of these, when the pulmonary blood flow was increased by operation, the curve tended to move back towards normal. This " shift to the right " is assumed to be a compensatory mechanism, whose mode of origin, however, is unknown.
P. Mestitz

576. **The Clinical Significance of Cold Agglutinins.** (Клиническое значение холодовых агглютининов)
E. M. TAREEV and M. V. DOROGOVA. Терапевтический Архив [*Terap. Arkh.*] **22**, No. 4, 29–41, July-Aug., 1950. 7 refs.

Cold agglutinins were studied in 38 healthy and 242 sick subjects. The findings in 44 cases are tabulated, 4 case histories are given in detail, and the whole series is discussed.

Of serum samples from 38 healthy subjects, 3 had cold agglutinin titres of 1 in 10 to 1 in 15, and 31 had titres not exceeding 1 in 8; in 4, cold agglutinins were not found. The cold agglutinins in the healthy subjects had a temperature range of 0° to 8° C.

Patients with blood diseases tended to have high titres in the serum. In haemolytic anaemia titres were high, but the amount of cold agglutinins fell after splenectomy. In a case of Raynaud's syndrome the titre was 1 in 2,800, the highest value in the series. Cardiovascular disease was accompanied by an increase in cold agglutinins in the serum, if active inflammation was still present. Cirrhosis of the liver and protozoal disease, especially visceral leishmaniasis, were accompanied by a rise in cold-agglutinin titre. High titres were also common in acute infections and in those diseases of the gut leading to anaemia or avitaminosis. The temperature range of cold agglutination was widened only in cirrhosis of the liver and in the Raynaud syndrome.

A rise in cold-agglutinin titre does not contraindicate blood transfusion, but is an additional reason for warming the blood before administration. *Jeffrey Boss*

577. **A Modification of *in vivo* Estimation of Hyaluronidase.** (Odmiana metody oznaczania hialuronidazy *in vivo*)
B. ZABLOCKI. *Polski Tygodnik Lekarski* [*Polsk. Tyg. lek.*] **5**. 922–923, June 12, 1950. 2 refs.

Because of discrepancies in the results of estimation of hyaluronidase *in vivo* in the usual way, the author suggests a new method. A female rabbit, epilated mechanically, is given an intradermal injection of 0·2 ml. of the solution to be examined; as a control saline, or a boiled filtrate of *Staphylococcus*, is used in estimating hyaluronidase in testicular extracts or *Staphylococcus aureus* filtrates respectively. The time of flattening of the skin elevation is recorded. A time less than 25% of that for the control indicates a positive result. The advantages of the method are: (1) its simplicity; (2) accuracy in recording; (3) short duration (less than one hour). *J. W. Czekalowski*

578. **The Value of Clinical Laboratory Tests. II. The Excretion of Total Neutral 17-Ketosteroids in Disease**
H. GREENBURGH, W. H. H. MERIVALE, A. TICKNER, and D. WATSON. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **99**, 165–177, 1950. 1 fig., 29 refs.

The excretion of total neutral 17-ketosteroids has been estimated in 30 normal subjects and 92 patients with a variety of clinical disorders. Results obtained for excretion in normal subjects agreed well with those in the literature. Increased excretion was found in patients with suprarenal cortical carcinoma, benign hirsutism, inconstantly in Cushing's syndrome, and in one patient with a pituitary tumour. Excretion was decreased in patients with Addison's disease, acromegaly, anorexia nervosa, and in certain forms of cardiac disease unassociated with any endocrine lesion.—[Authors' summary.]

579. **Studies on Effusions. I. Glucuronidase and Lactic Acid in Neoplastic Effusions of Pleura and Peritoneum**
W. H. FISHMAN, R. L. MARKUS, O. C. PAGE, P. H. PFEIFFER, and F. HOMBURGER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220**, 55–59, July, 1950. 2 figs., 9 refs.

Lactic acid and β-glucuronidase determinations, together with cytological examinations, were carried out on 106 effusions from the pleura and peritoneum, obtained from 40 cases of cancer, and on a very small control group of 9 samples of transudates from 8 patients with liver disease or cardiac decompensation. The lactic acid and glucuronidase values in the latter group ranged from 11 to 42 mg. per ml. and 95 to 393 units per 100 ml. respectively, and no cells, apart from an occasional mesothelial cell, were seen in the fluid.

Of the 106 neoplastic effusions (lactic acid range 5 to 200 mg. per ml., and glucuronidase activity from 0 to 8,250 units), 45 contained no cells and 13 gave glucuronidase and lactic acid values no higher than those in the control group. Of the 45 specimens of proven cancer in which cytological studies gave negative results 28 had a glucuronidase activity and 16 a lactic-acid concentration above the average for the control group.

Positive cytological findings alone were not always accompanied by an elevated concentration of lactic acid and glucuronidase, and their elevation was not invariably accompanied by the presence of detectable tumour cells.

The chemical and cytological characteristics of ascitic fluid from one patient with cancer, studied at intervals over a period of 9 weeks, changed spontaneously without any apparent correlation with the clinical severity of the disease. The authors discuss mechanisms which might explain the variability in the composition of neoplastic effusions. *R. P. Hullin*

580. **Determination of Proteins, Albumin, Globulin, and Fibrinogen by Means of the Ring Formation between a Serum Layer and Nitric Acid.** (Определение содержания общего белка, альбумина, глобулина и ориентировочное определение фибриногена в крови по образованию кольца при наслаивании сыворотки на азотную кислоту)
E. A. MJUL'KIJAN. Терапевтический Архив [*Terap. Arkh.*] **22**, No. 4, 65–69, July–Aug., 1950. 1 fig.

The time taken for the formation of a ring between layers of concentrated nitric acid and of diluted serum under standard conditions is noted. The concentration of protein in the serum can then be found from this, at the serum dilution used, from a table provided. The amounts of various plasma protein fractions are calculated from estimations made before and after differential precipitation. *Jeffrey Boss*

581. **Red Cell and Plasma Volume in New-born Infants**
P. L. MOLLISON, N. VEALL, and M. CUTBUSH. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **25**, 242–253, Sept., 1950. 4 figs., 21 refs.

582. **Some Difficulties in the Interpretation of Haematological Data, with Particular Reference to the Estimation of Capillary Fragility**
J. H. BOLTON. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 256–259, Aug. 12, 1950. 3 figs., 8 refs.

The number of petechiae produced in a circular area of the skin of the forearm 3 cm. in diameter after 5 minutes of venous occlusion was determined on 354 occasions in 69 cases of diphtheria. On analysing the results there was a marked asymmetry of the frequency distribution, which made it difficult to apply the usual statistical methods of evaluation. The distribution of petechiae in different areas of the forearms during one test on a single case was of the Poisson form, but this did not apply to the figures from the whole group. The distribution of a negative binomial, however, provided a close fit, and by means of a transformation formula suggested by Bartlett each figure was converted to a new form in which the distribution was much more symmetrical, and it was then possible to use the usual methods of analysis. There was found to be a significant correlation between occlusion pressure and number of petechiae, and an "adjusted petechial index", having a normal distribution, was obtained by means of the linear regression equation derived from the correlation data. It is pointed out that the negative binomial distribution

should, in theory, be widely applicable in the enumeration of rare events occurring in variable or non-homogeneous material. In haematology, for example, it describes the distribution of megakaryocytes in the bone marrow, and of eosinophils in the differential leucocyte count.

[The original paper should be consulted for the formulae used.] *M. Lubran*

583. **The Effect of Venous Compression on Certain Blood Factors**
T. J. BERRY, E. PERKINS, and P. JERNSTROM. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **20**, 765–767, Aug., 1950. 12 refs.

It has long been known that compression of a vein by a tourniquet, such as is used in normal venepuncture technique, causes increased capillary filtration, with retention of protein and cells and haemoconcentration in the vein distal to the occlusion. To determine the clinical significance of such changes in relation to the collection of blood specimens for chemical analysis, tests were made on a mixed group of 30 patients, to whose arms a tourniquet was applied at a pressure of 60 mm. Hg, blood samples being taken without suction after 2 minutes, and again after 5 minutes, a control sample having been taken before constriction. Haematocrit value, serum protein level, specific gravity, and haemoglobin value were estimated in all three samples in each case. All the values were increased by application of the tourniquet, those obtained after 5 minutes' compression being higher than those after 2 minutes. However, the greatest increase, which was in the haematocrit reading, was only 6% higher than the control value, so that any error occasioned by this technique is well within the bounds of experimental error and it is therefore concluded that there is no serious contraindication to the use of a tourniquet in the obtaining of blood samples for routine pathological tests. *A. Michael Davies*

584. **Plasma Protein Studies of 200 Cases of γ-Hyperglobulinaemia and their Clinical Application.** (Über Bluteiweissuntersuchungen bei 200 Krankheitsfällen von γ-Hyperglobulinämie und ihre klinische Bedeutung)
F. WUHRMANN, C. WUNDERLY, and P. DE NICOLA. *Zeitschrift für Klinische Medizin* [*Z. klin. Med.*] **147**, 73–100, 1950. 9 figs., bibliography.

Electrophoretic analysis of sera in 24 cases of myelomatosis revealed a significant decrease in γ-globulin mobility compared with 8 normal sera. In 23 cases of hepatic disease, tuberculosis, or malignant disease, there was no change. Electrophoretically homogeneous γ globulin was prepared in 8 cases of myelomatosis by methanol precipitation of the sera at *p*H 6·8 in the cold. Extinction coefficients, at 280 mμ. and *p*H 2 and >12, differed widely, lying above and below the normal. These results support the hypothesis of the heterogeneity of the γ globulins. In the electrophoretic patterns, the peaks of myeloma γ globulin were steeper and narrower than corresponding peaks in other diseases. The authors consider the shape of the peak to indicate the degree of heterogeneity of the γ globulins, the ratio of height to width of base (Q) decreasing with increasing heterogeneity.

Out of 800 sera analysed by electrophoresis, 200 had a raised γ-globulin content, that is, this globulin formed more than 20% of the total protein (normal=14 to 18%). In each case, the diagnosis and the figures for protein and Q are recorded. In 150 cases the cadmium sulphate turbidity test and Weltmann calcium chloride heat-coagulation test were performed.

In myelomatosis, γ globulin forms about 40% of the total protein, the amount of the latter being also raised. The cadmium reaction is positive and there is a marked shift to the right in the Weltmann reaction. The empirical protein reactions are strongly positive. The erythrocyte sedimentation rate is typically raised and Q is increased, this change being almost pathognomonic.

In malignant disease all three globulin fractions increase, but there is a subnormal or low value for total protein. The cadmium reaction is positive and there is a shift to the left in the Weltmann test.

In alcoholic cirrhosis of the liver the amount of γ globulin is moderately increased, while those of α and β globulin are slightly raised. The cadmium reaction is positive and the Weltmann test shows a widened range of coagulation. In acute infections α globulin increases in amount as well as γ globulin. In chronic infections the results are variable. *M. Lubran*

585. **The Erythrocyte Sedimentation Rate in Defibrinated Blood.** (Opadanie krwinek we krwi odwłóknionej)
E. GORZKOWSKI. *Gruźlica* [*Gruźlica*] **18**, 90–101, Jan.–March, 1950. 3 figs., 20 refs.

Experiments on the erythrocyte sedimentation rate (E.S.R.) were carried out with defibrinated blood alone and defibrinated blood together with sodium citrate; as a control whole citrated blood from the same individual was used.

It is concluded that: (1) the E.S.R. chiefly depends upon the factors influencing the formation of rouleaux and aggregates of erythrocytes; (2) the E.S.R. is directly related to the size of these rouleaux or aggregates; (3) defibrination deprives the blood of a factor responsible for the accumulation of erythrocytes; (4) comparison of the E.S.R. in whole citrated blood with that in defibrinated blood provides a guide to the state of the plasma proteins.

The author describes a case of multiple myeloma with a high E.S.R. The cross-sedimentation test with the patient's erythrocytes and plasma from a case of polycythaemia vera, and vice versa, revealed that the factor responsible for the high E.S.R. in this case was confined to the plasma. *J. W. Czekalowski*

586. **Metabolism and Excretion of Alkaline Phosphatase: Relation to Liver Function and Determination of Maximal Secretory Rates of Liver**
H. H. LEVEEN, L. J. TALBOT, M. RESTUCCIA, and J. R. BARBERIO. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 192–205, Aug., 1950. 8 figs., 25 refs.

Alkaline phosphatase was injected intravenously in doses of 200 Bodansky units into 8 dogs with duodenal fistulae, the preparation of alkaline phosphatase used,

which was obtained from calves' duodenum, having an activity of 75 to 100 Bodansky units per ml. at *p*H 9·1. The serum phosphatase level rose to a maximum of about 30 units per 100 ml. within 30 minutes and returned to normal (3·5 to 7·5 units) in 1 to 1½ hours. The concentration of phosphatase in bile, collected at the same time by cannulation of the common duct, reached a maximum of about 300 units per 100 ml. in 1½ to 2 hours and returned slowly to normal (5 to 15 units per 100 ml.) during the next 96 hours. In 2 dogs the whole dose was excreted into the bile. The rate of excretion of phosphatase in the bile rapidly rose to a maximum constant level of 6 units per hour and was independent of the blood phosphatase level. An injection of 1 g. of phloridzin into one dog caused an almost complete abolition of phosphatase excretion into the bile.

It was shown in 4 dogs by means of liver biopsy and special staining techniques that injected phosphatase was taken up completely by the liver and was located in the polygonal cells, being in greater concentration in those parts adjacent to the bile canaliculi. None was taken up by the reticulo-endothelial cells, nor was there any prolongation of the rise in serum phosphatase level following injection into animals in which the reticulo-endothelial system had been blocked with indian ink. In one dog which developed liver damage the maximum rate of excretion of phosphatase into the bile after injection was normal. In another dog, following cholecystectomy and the production of an acute biliary fistula, phosphatase excretion into the bile continued at the maximum rate long after the injected dose had been excreted. In 2 dogs there was evidence of absorption of a small part of the phosphatase from the small intestine.

M. Lubran

587. **Studies in *para*-Aminohippuric Acid Synthesis in the Human: its Application as a Liver Function Test**
W. P. Deiss and P. P. Cohen. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1014–1020, Aug., 1950. 4 figs., 17 refs.

In the investigation of hepatic function the hippuric-acid test has the drawback of requiring a relatively normal renal excretion. To overcome this difficulty, the authors have developed a new test based on the synthesis of *para*-aminohippuric acid (PAH) from *para*-aminobenzoic acid (PAB) when given orally. They used the diazo-coupling reaction for analysis of sulphonamides after ether extraction of PAB in studying the process of synthesis of PAH and found that the serum level of PAH varied with the state of liver function. The serum PAH level one hour after ingestion of 3 g. of sodium PAB was determined in 60 healthy subjects and a mean value established. The serum PAH level, expressed as the percentage of this normal mean, was consistently below 100 (range 7·1 to 58·4) in 13 patients with primary liver disease, indicating a reduction in PAH synthesis. Impairment of synthesis was also noted in 3 patients with secondary malignant disease of the liver (values 60 to 66·5%), 2 cases of chronic ulcerative colitis (32·8% and 34·6%), 3 cases of thyrotoxicosis (49%, 53%, and 64%), 2 cases of rheumatoid arthritis (53% and 56%), and in 10 out of 11 cases of infectious mononucleosis (range 29% to 78·5%). The value was normal (87% to 96%) in 5 out of 7 patients with obstructive jaundice, slightly diminished (70%) in 1, and abnormally low (54·5%) in the seventh. Administration of glycine appreciably increased PAH synthesis in 8 normal subjects.

A. I. Suchett-Kaye

588. **A Flocculation Test with Double Distilled Water.** (Prueba de floculación con agua bidestilada)
J. Cabello and S. Silva. *Revista Médica de Chile* [*Rev. méd. Chile*] **78**, 445–451, July, 1950. 2 figs., 8 refs.

From work performed on 50 normal individuals and 875 patients in the Salvador Hospital, Chile, the authors show that dilution of blood serum to 1 in 20 with double-distilled water produces a turbidity which can be measured photometrically in thymol units, and may cause obvious precipitation. Normal sera in 24 hours show a turbidity of 1 to 2 thymol units with no precipitation. Sera in cases of disease give values of 2 or more and frequently show precipitation. The test gave results in agreement with those of other flocculation tests used in the differential diagnosis of jaundice. The test is compared with the thymol-turbidity test, and it is shown that there is a definite indirect correlation between the intensity of turbidity and the albumin : globulin ratio.

René Méndez

589. **Anomalous Findings in Differential Diagnosis of Jaundice by Biochemical Tests**
P. N. Coleman. *British Medical Journal* [*Brit. med. J.*] **2**, 246–248, July 29, 1950. 9 refs.

The application of Maclagan's scheme, involving the estimation of serum alkaline phosphatase and the thymol-turbidity test as aids in the diagnosis of jaundice, was investigated in 46 cases of non-obstructive jaundice and 24 cases of obstructive jaundice.

When Maclagan's criteria were applied (low alkaline-phosphatase level and/or strongly positive thymol turbidity indicating nonobstructive jaundice, whereas high alkaline-phosphatase level combined with a negative or weakly positive turbidity reaction indicates obstruction) the correct diagnosis was made in 33 out of the 46 cases of non-obstructive, and in 18 of the 24 cases of obstructive jaundice. In 15 cases the result was equivocal, while 3 cases of hepatitis and one of cirrhosis were incorrectly classified as cases of obstructive jaundice.

The addition to the routine of qualitative tests for urine urobilinogen and a serum albumin and globulin estimation enabled a firm diagnosis to be made in 3 of the 15 cases of equivocal results and indicated the correct diagnosis in the 4 cases wrongly classified, besides confirming, in many cases, the diagnosis already made by Maclagan's criteria.

It is suggested that exceptions are more likely to occur to the criteria for the diagnosis of obstructive jaundice than to those given for non-obstructive cases. While the urobilinogen and serum protein tests pointed to the correct diagnosis in the 4 cases with anomalous findings in the series reviewed, the author agrees that the numbers are too small for any final conclusion to be drawn about the value of inclusion of these tests.

R. P. Hullin

Microbiology

VIRUSES

590. **Isolation of a Common Cold Virus in Chick Embryos and the Clinical Manifestations it Produces in Human Volunteers**
T. G. WARD and D. F. PROCTOR. *American Journal of Hygiene* [*Amer. J. Hyg.*] **52**, 91–106, July, 1950. 22 refs.

Nasal washings were taken up in 10 ml. of heart-infusion broth from subjects during the early stages of an acute cold. Without filtration, quantities of 0·25 to 0·4 ml., together with 250 units penicillin and 2,500 μg. streptomycin, were inoculated into the allantoic sac of 7-day chick embryos. These were incubated for 6 days at 35° C. in an atmosphere of 90% humidity. The fluid from 10 to 12 embyros was pooled, diluted 1 in 1,000, and inoculated into another series of 7-day embryos, the process being carried through until the fifth passage had been reached. By this method a strain of virus designated WW was isolated.

A pool was made from 40 bacteriologically sterile specimens of fluid of the fifth passage, distributed into ampoules, and frozen in dry ice. Four to 9 weeks later inoculation experiments were carried out on male volunteers in a State Reformatory. They were housed in two isolation wards each containing ten beds.

Volunteers were inoculated by dropping 0·5 ml. of allantoic fluid into each nostril on two occasions 6 hours apart. Control material consisted of the same pool of allantoic fluid after autoclaving, or a mixture of such fluid and fluid from non-infected eggs. Three separate studies were made; out of a total of 23 test inoculations 14 resulted in clinically recognizable colds, whereas only one doubtful cold resulted from inoculation of control material into 24 subjects. The incubation periods were: in 11 cases, 40 hours, in 2 cases 72 hours, and in one case 96 hours. *R. Hare*

591. **The Use of Radioactive Phosphorus in Studies of Chick Embryo Infections with a Common Cold Virus**
T. G. WARD. *American Journal of Hygiene* [*Amer. J. Hyg.*] **52**, 107–132, July, 1950. 2 figs., 25 refs.

In view of the fact that there is no method other than inoculation of human volunteers by which the presence of common cold virus in the allantoic fluid of hens' eggs may be detected, experiments were carried out to determine whether alterations in the phosphorus metabolism of virus-containing eggs, as indicated by the distribution of ^{32}P, could be employed for this purpose.

The ^{32}P employed was in the form of NaH_2PO_4 brought to neutrality by the addition of alkali and diluted in such a way as to give counts of one million to five million per minute per 0·1 ml. in the Geiger counter. This quantity was put in the allantoic sac of egg embryos, 7 to 8 days old, and immediately afterwards the virus (WW cold virus or mumps virus) or control diluent was inoculated. The allantoic fluid from groups of five living embryos at intervals of 12 to 16 hours thereafter was harvested.

By a modification of the Schneider (*J. biol. Chem.*, 1945, **161**, 83) method, the acid-soluble phosphorus, the phospholipids, the ribose nucleic acid, and the desoxyribose nucleic acid fractions of the fluids were isolated. The ratio of counts per minute of phosphorus in the ribose nucleic acid fraction to counts in the acid-soluble phosphorus compound was then determined. In eggs infected by common cold virus WW, this ratio was 10 to 30 times greater than in control preparations. Similar changes were detected in eggs infected with the PR 8 strain of influenza-A virus and two strains of mumps virus. *R. Hare*

592. **The Haemolytic Action of Newcastle Disease Virus. I. The Two Types of Interaction between Virus and Red Cell**
F. M. BURNET. *Australian Journal of Experimental Biology and Medical Science* [*Aust. J. exp. Biol. med. Sci.*] **28**, 299–309, May, 1950. 12 refs.

593. **A Complement Fixation Test for Herpes Simplex Infections**
J. A. DUDGEON. *Journal of Clinical Pathology* [*J. clin. Path.*] **3**, 239–247, Aug., 1950. 24 refs.

BACTERIA

594. **Experimental Study of Staphylococcal Toxins and Anatoxins.** (Экспериментальное изучение стафилококковых токсинов и анатокснов)
S. S. LUR'E. Вестник Венерологии и Дерматологии [*Vestn. Vener. Derm.*] No. 4, 16–18, July–Aug., 1950.

Of 115 strains of staphylococci investigated only one was found to produce a toxin *in vitro*. This toxin had marked haemolytic and necrotizing activity, and was of high antigenicity. A toxoid was prepared from it by the addition of 0·4% of formalin; its immunizing power was tested in rabbits, giving up to 5 injections at intervals of 5 or 6 days, and similar experiments were carried out with staphylococcal vaccine for purposes of comparison. The immune state of the animals was investigated by the injection of toxin or living staphylococci, and by the determination of serum antibody titres. High blood levels of antitoxin were produced by the injection of the toxoid, and the animals resisted the intravenous injection of lethal amounts of toxin; the titres fell off after 2 months or so, but rose again after a further injection. Staphylococcal vaccine did not produce antitoxin; rabbits immunized with it still gave a necrotic skin reaction after intradermal inoculation of living staphylococci, whereas rabbits immunized with formol-toxoid gave only a negligible reaction and showed a high resistance to infection. *D. J. Bauer*

595. **The Classification of the Coli-aerogenes Bacteria**
REPORT OF THE COLIFORM SUB-COMMITTEE, SOCIETY FOR GENERAL MICROBIOLOGY AND SOCIETY FOR APPLIED BACTERIOLOGY. *Proceedings of the Society for Applied Bacteriology* [*Proc. Soc. appl. Bact.*] **2**, 3–16, 1949. 16 refs.

The classification of the coli-aerogenes group of the genus *Bacterium* now put forward separates them into six main groups on the basis of indole production, methyl red and Voges–Proskauer reactions, and citrate utilization:

Group	Indole	M.R.	V-P.	Citrate
I	+	+	−	−
II	−	+	−	−
III	−	+	−	+
IV	+	+	−	+
V	−	−	+	+
VI	+	−	+	+

Bacterium aerogenes type I falls into Group V: *B. aerogenes* type II into Group II. *G. M. Findlay*

596. **Development of Chloramphenicol-resistant and Chloramphenicol-dependent Variants of a Strain of *Klebsiella pneumoniae***
T. M. GOCKE and M. FINLAND. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 824–829, Aug., 1950. 5 refs.

A strain of *Klebsiella pneumoniae* was subcultured thirty times on a series of agar plates containing graded amounts of chloramphenicol. There was no increase in resistance for the first 6 subcultures, and at this time growth was completely inhibited by 3·1 μg. of antibiotic per ml. and partially inhibited by 1·6 μg. per ml. A progressive increase in resistance occurred between the 6th and 22nd subcultures, and between the 22nd and 30th transfers the organism was completely inhibited by 800 μg. per ml. and partially inhibited by 200 μg. per ml. At each stage the organism was also subcultured on antibiotic-free agar. The 14th to the 17th of these subcultures were found to consist largely, if not wholly, of micro-organisms which required chloramphenicol for growth. It was also found that: (1) these dependent organisms required a minimum of 3·1 μg. or more of chloramphenicol per ml. of agar; (2) the optimum growth occurred on agar containing 12·5 or 25 μg. per ml.; (3) higher concentrations of antibiotic again inhibited growth. Evidence was also obtained of " back-mutation " to variants which were as sensitive as the parent strain. *A. W. H. Foxell*

597. **Sulphonamide Sensitivity of *H. influenzae* Strains, with Special Reference to the Combined use of Antibacterial Drugs**
K. ZINNEMANN. *British Medical Journal* [*Brit. med. J.*] **2**, 705–709, Sept. 23, 1950. Bibliography.

After reviewing some of the literature on the synergistic effect of two antibacterial agents acting together on a sensitive organism, the author considers the reports of a number of different observers on the combined treatment of *Haemophilus influenzae* meningitis. Especially striking are the excellent results with a combination of streptomycin and sulphonamides, although the addition of specific type-B antiserum may be of great value on occasions.

Sensitivity was tested of a number of capsulated and non-capsulated (50 each) strains of *H. influenzae* to the action of a standard concentration of sulphanilamide, sulphapyridine, sulphathiazole, sulphadiazine, sulphamezathine, sulphamerazine, and " marfanil " (maphenide). The tests were carried out by two methods: by inoculation of media with which was incorporated the particular sulphonamide tested, and by the punch-plate technique, which is simpler but yields less accurate results. In concentrations of 10 mg. per 100 ml., sulphathiazole was the most effective single sulphonamide tested, followed by sulphadiazine, sulphamezathine, and sulphamerazine, but " sulphatriad " (a mixture of sulphathiazole, sulphadiazine, and sulphamerazine), appeared to be more effective than any of its single constituents. Generally the capsulated strains were less sensitive to the action of the sulphonamides than the non-capsulated strains. Since the sensitivity tests of individual strains may show that a particular member of the group is active against another strain, it is specially important that each strain isolated from clinical cases be tested for sulphonamide sensitivity to ensure the maximum therapeutic effect. *H. J. Bensted*

598. **Streptomycin Resistance of *Mycobacterium tuberculosis* in Tuberculous Meningitis.** (Streptomycin-resistenz des *Mycobacterium tuberculosis* bei Meningitis tuberculosa)
F. J. POTHMANN and K. O. FEHR. *Zentralblatt für Bakteriologie, Parasitenkunde und Infektionskrankheiten. 1 Abt., Originale* [*Zbl. Bakt.* (1 *Abt., Orig.*)] **156**, 67–80, Aug. 15, 1950. 2 figs., 44 refs.

The authors examined 43 strains of tubercle bacilli, isolated from the cerebrospinal fluid (C.S.F.) of 43 children, with regard to streptomycin sensitivity and resistance, and also with a view to obtaining some information on the combined use of streptomycin and thiosemicarbazone. Strains growing in a concentration of 10 to 14 μg. of streptomycin per ml. of medium were regarded as resistant. Owing to difficulties in obtaining certain ingredients of Dubos's medium, a fluid medium developed in Germany by Hermann (*Z. Hyg.*, 1949, **129**, 103 and 146) and giving good results was used. The strains isolated were mostly of the human type [proportion of human to bovine strains not stated]. Seven strains were sensitive to 1 μg. or less of streptomycin per ml., 22 strains were relatively sensitive to 1 to 10 μg. per ml., and 14 strains were resistant. In 4 additional cases the development of resistance could be observed during treatment. The sensitivity of the strains before and after treatment in these cases was 0·8 and 12·5, 12·5 and 100, 12·5 and 25·0, and 1·5 and 3·0 μg. per ml. respectively. On the other hand, 4 strains could be cultured only 5 to 12 months after starting streptomycin treatment and their sensitivity ranged from 0·8 to 6·0 μg. per ml.

Of 15 children from whose C.S.F. resistant strains were cultured, 6 were still alive after more than 8 months of treatment. One of these children was discharged as cured, the result in 3 further children was good, another one had a relapse, and one developed hydrocephalus. Of 28 children from whose C.S.F. strains with normal sensitivity were cultured, 7 died, but these children were admitted to hospital in a very advanced stage of the disease. Seventeen of the remaining 21 children were well, although treatment was still going on at the time of the report, and 3 of these 17 children had had several relapses. In 3 of the other cases the prognosis was doubtful and in one poor. The vast majority of strains from surviving children showed normal or relative sensitivity, while most strains from fatal cases showed high resistance. The success of treatment did not necessarily depend on the institution of streptomycin therapy at an early stage of the disease, nor was the streptomycin sensitivity dependent on the length of time elapsed between the start of illness and the beginning of treatment. Experiments *in vitro* with 30 strains of *Mycobacterium tuberculosis* showed a marked synergism of action between streptomycin and thiosemicarbazone.

[The discussion with regard to the development and prevention of streptomycin resistance is not quite up-to-date, little attention having been paid to the various papers of American authors explaining these phenomena in terms of bacterial genetics.] *K. S. Zinnemann*

599. **Studies on the Gelatin-liquefying Properties of Certain Bacteria, with Particular Reference to the Laboratory Diagnosis of Cystic Fibrosis of the Pancreas**
D. E. JOHNSTONE. *Pediatrics* [*Pediatrics*] **6**, 351–356, Sept., 1950. 1 fig., 9 refs.

600. **Simplified Fluorescence Microscopy of Tubercle Bacilli**
E. MATTHAEI. *Journal of General Microbiology* [*J. gen. Microbiol.*] **4**, 393–398, Sept., 1950. 4 figs., 7 refs.

IMMUNITY

601. **Diffusible Antigens in Staphylococcal Cultures**
S. D. ELEK and E. LEVY. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **31**, 358–368, June, 1950. 4 figs., 11 refs.

A series of 359 strains of *Staphylococcus* were grown on "difco" heart-infusion broth-haemolysed horse-erythrocyte agar in which a rectangular filter-strip soaked in staphylococcal antiserum had been embedded. The strains were streaked on the medium at right angles to the filter strip and the plates incubated for 4 days at 37° C. in an atmosphere of 30% CO_2 and 70% air; final readings were taken after a further 48 hours at room temperature. In accordance with the double-diffusion-gradient principle, antigens to which a specific antibody was present in the serum flocculated with that antibody as they diffused from the staphylococcal colony; a "line" thus developed in the medium. The number of lines formed in this way is (with certain qualifications) an index of the number of soluble antigens formed by the organism.

All coagulase-positive strains produced lines when grown at right angles to a filter-strip containing antiserum against the Wood 46 strain; no lines were produced by any coagulase-negative strain. The mean number of lines produced by animal pathogens was less than the mean number produced by human pathogens; coagulase-positive strains from skin produced fewer lines than strains from lesions.

While penicillin resistance and lesions of origin bore no relation to the number of lines produced, increasing degrees of pigmentation, mannitol fermentation, and gelatinase production were associated with a significant increase in the mean number of lines.

[The authors make it clear that no more lines can be produced than there are antibodies in the serum used: since the antigens produced by different strains might vary greatly in nature as well as number, this might seriously affect the result obtained. It would be extremely interesting to compare the results here recorded with those obtained with the same strains when an antiserum prepared by immunizing animals against filtrates of coagulase-negative staphylococci was used: might not the coagulase-positive staphylococci fail to give lines? It would perhaps be unreasonable to ask the authors to attempt to decide whether their strains can be grouped by their capacity to produce one or more common antigens, though their methods afford a means of doing this; the labour involved would be enormous. Nevertheless, the fact that the method demonstrates only the number of antigens (and even this with reservations) without discriminating in any way between them, is an obvious defect.] *C. L. Oakley*

602. **The Role of Bacterial Antigens in Diphtheria Prophylactics**
I. SCHEIBEL. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **31**, 442–448, June, 1950. 16 refs.

The assessment of the relative merits of a purely antibacterial and a purely antitoxic immunity to *Corynebacterium diphtheriae*, and of a combination of both, has only recently become possible through the production of diphtheria toxin and toxoid preparations which are free from other protein fractions, and the development of a technique of infecting guinea-pigs whereby a lesion resembling the human diphtheritic membrane is produced in a cutaneous focus of infection. The latter procedure is as follows: a small area of skin of the abdominal wall is shaved and gently scarified; a small amount of a virulent broth culture of *C. diphtheriae* is rubbed on to the scarified area, which is then covered with a piece of gauze moistened with saline and kept in position by means of adhesive tape, a typical diphtheritic membrane with local oedema developing and death occurring in 2 to 5 days.

The purified toxoid used in the experiments reported here from the State Serum Institute, Copenhagen, was adsorbed on to aluminium hydroxide to give a final concentration of 1 mg. Al and 50 Lf of toxoid per ml. The bacterial vaccine used was prepared from *C. diphtheriae gravis* strain No. 1282, grown on ascitic-fluid

agar for 48 hours, the medium containing ferrous sulphate in order to reduce toxin production to a minimum. The same strain was also used to infect guinea-pigs cutaneously as described. A practically toxin-free culture-filtrate protein fraction was obtained by growing the P.W.8 strain on a Pope medium with an added excess of iron, and was adsorbed on aluminium hydroxide in the same way as the toxoid.

In a first series of experiments one group of guinea-pigs was given two injections of 0·2 ml. of the purified diphtheria toxoid at 4 weeks' interval, a second group was immunized in the same way and received in addition 8 intraperitoneal injections of vaccine, increasing from 12,000,000 to 100,000,000 organisms, at 3 to 4 days' intervals, and a third group was given the bacterial vaccine alone. One week after the 2nd injection of toxoid and 4 days after the last dose of vaccine the antitoxin and agglutination titres of the blood were determined, and on the following day the treated animals and two groups of fresh control guinea-pigs were infected in the way described. As expected, the first group showed a purely antitoxic, the third a purely antibacterial, and the second a combined response. Only the animals possessing a sufficiently high antitoxin titre survived. In the second series of experiments two additional groups of treated animals were introduced and the immunizing dose of toxoid reduced to one injection of 1 Lf, the aim being to examine the effect, if any, of the non-toxic protein fraction of toxoid and to avoid excessive immunization which might mask slight immunization by the vaccine. The first additional group received three subcutaneous injections of the non-toxic protein fraction at weekly intervals together with one dose of 1 Lf of toxoid, and the second additional group were given three injections of the non-toxic fraction alone. The other 3 groups of animals corresponded to the experimental groups in the first series. All animals which were immunized with toxoid acquired increased resistance to the infection, and no correlation was found between agglutination titres following vaccination with bacterial vaccine or non-toxic protein fraction and survival. Animals showing an insufficient response to the 1-Lf dose of toxoid nevertheless developed high antitoxin titres under the stimulus of infection. The author considers that elimination of proteins of a non-specific nature from diphtheria prophylactics, in an attempt to avoid reactions, seems justified. *K. S. Zinnemann*

603. **Immediate (So-called " Immune ") Reaction to Smallpox Vaccination**

A. S. BENENSON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 1238–1240, Aug. 5, 1950. 2 figs., 37 refs.

A large group of U.S. Army Medical Department officers, all of whom had been vaccinated against smallpox one or more times previouly, were re-vaccinated on one arm with living virus from one of two sources, and on the other with the same virus inactivated by heating the sealed capillary containing the virus in a constant-temperature water-bath for ½ or 3½ hours at 56° C., or at 60° C. for one hour. The multiple-pressure method was used, with precautions to prevent cross-infection, and reactions were recorded on the 1st, 2nd, 3rd, 4th, 8th, and 14th days. Reactions reaching their maximum in less than 72 hours were classed as " immediate ", those at their height between the 4th and 7th days as " vaccinoid ", while those maximal after the 7th day were labelled " vaccinia ". All reactions were further classified as (*a*) papular, (*b*) areolar, (*c*) vesicular, or (*d*) areolo-vesicular, in accordance with usual practice.

The reactions to live virus, when they occurred, were all vaccinoid: 8 subjects gave no reaction to live virus, but inactivated virus produced an immediate reaction, while in 3 persons the reverse was the case. Of the 56 persons showing an immediate reaction to both injections, in 29 the reactions were of similar character, while in 11 a more severe reaction was produced by the inactivated virus. Reactions to inactivated virus were occasionally severe, leading to the early development of an areola and vesiculation.

The author concludes that the state of immunity to smallpox cannot be estimated by the reaction of the subject to heated vaccinia virus, and suggests that the terms " immune reaction " and " reaction of immunity " should be abandoned and replaced by " immediate reaction " when the maximum is reached within 72 hours.

[This paper reminds one that the changes occurring when protein solutions or suspensions of virus are heated are far from perfectly understood.] *C. L. Oakley*

604. **Factors Influencing the Agglutinability of Red Cells: The Demonstration of a Variation in the Susceptibility to Agglutination Exhibited by the Red Cells of Individual Oxen**

M. H. GLEESON-WHITE, D. H. HEARD, L. S. MYNORS, and R. R. A. COOMBS. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **31**, 321–331, June, 1950. 9 refs.

The erythrocytes of individual oxen show marked variation in the degree to which they are agglutinated by antiglobulin sera after they have been sensitized with infectious-mononucleosis sera or rabbit anti-ox-erythrocyte sera; the cells of some oxen are not agglutinated at all by antiglobulin sera, though they may be shown to have absorbed as much Paul–Bunnell " antibody " or anti-ox-erythrocyte antibody as cells that are completely agglutinated, and though they are readily lysed in the presence of guinea-pig complement. The property appears to be characteristic of the cells, independent of the sera used; more than one antigen site is involved. Sensitized cells that fail to agglutinate with antiglobulin sera may still be agglutinated by treatment with trypsin.

[It looks as if, when sera are being titrated by these methods, the inclusion of a standard serum would be of value.] *C. L. Oakley*

605. **The Demonstration of Complement-fixing Antibodies to Herpes Febrilis Virus**

M. FLOWER. *Australian Journal of Experimental Biology and Medical Science* [*Aust. J. exp. Biol. med. Sci.*] **28**, 339–342, May, 1950. 9 refs.

Paediatrics

606. **The Influence of Adrenal Cortical Hormone on the Carbohydrate Metabolism of the Newborn.** (Über den Einfluss des Nebennierenrindenhormons auf den Kohlenhydratstoffwechsel des Neugeborenen)
J. ERBSLÖH and H. MERTENS. *Zeitschrift für Geburtshilfe und Gynäkologie* [*Z. Geburtsh. Gynäk.*] **133**, 158–171, 1950. 5 figs., bibliography.

The authors confirm that, in the newborn, blood sugar levels are very low (30 mg. per 100 ml. or less) during the first day after delivery without giving rise to hypoglycaemic symptoms. Injection of 5 mg. of deoxycortone (desoxycorticosterone) acetate or similar preparation into infants daily during 8 days caused no great change in blood sugar level. In further investigations, the authors determined the sugar tolerance after giving 7 g. of dextrose by mouth. The maximum height of the curve was reached in 90 minutes; after 135 minutes, however, the blood sugar had not returned to its original level. After injection of deoxycortone acetate the maximum height was reached after 45 minutes, and after 90 or 135 minutes the blood sugar level was far below the original.

The authors explain the action of deoxycortone acetate as creating an increased avidity of the tissues for sugar and improving the assimilation of glucose. The effect of this preparation is quite different from that of corticosteroids, which cause a rise in blood sugar level and increase the formation of liver glycogen. Furthermore, adrenal cortical extracts inhibit the action of insulin, but deoxycortone acetate acts like insulin.

Franz Heimann

607. **The Influence of Adrenal Cortical Hormone on Heat Regulation in the Newborn.** (Über den Einfluss des Nebennierenrindenhormones auf die Thermoregulation des Neugeborenen)
J. ERBSLÖH and F. SIEBERT. *Zeitschrift für Geburtshilfe und Gynäkologie* [*Z. Geburtsh. Gynäk.*] **133**, 172–181, 1950. 6 figs., 45 refs.

Heat regulation was studied in 24 babies after injection of deoxycortone acetate and the results were compared with those in 12 untreated babies. In both series the temperature was 37·4° C. (99·3° F.) after delivery and before ligation of the cord, and fell by 0·6° C. 4 to 5 minutes after ligation. The maximum fall was reached on an average after 1·5 hours and lasted for about 3·6 hours. The temperature became normal after 14 hours. Continuation of the injections for 3 to 4 days, however, produced a steadier temperature curve. If, on the other hand, the injections were given 1 to 2 hours before delivery, the initial fall in temperature and the thermolability were avoided. The authors are of the opinion that the drug has an influence upon the temperature-controlling centres in the hypothalamic region and in the tuber cinereum. *Franz Heimann*

608. **A Method of Collecting Total Excreta in Infants**
J. O. FORFAR and J. H. PRAIN. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **25**, 260–261, Sept., 1950. 3 figs., 2 refs.

609. **Use of Rectal Thiopentone in Children**
J. LORBER. *British Medical Journal* [*Brit. med. J.*] **2**, 21–22, July 1, 1950. 6 refs.

The methods of sedation most commonly employed by the paediatrician to enable him carry out certain painful or unpleasant diagnostic or therapeutic procedures are unsatisfactory for many purposes, especially in infants or when access to the face or prolonged sedation is required. Thiopentone has been administered per rectum for this purpose since the beginning of 1949 at the Children's Hospital, Sheffield, on 113 consecutive occasions to 64 children whose ages ranged from 3 months to 12 years, 11 being under one year old. Fifty-six were suffering from tuberculous meningitis, miliary tuberculosis, or other forms of tuberculosis. The indication for sedation was examination of the fundus oculi on 54 occasions, encephalography on 47, and other procedures on 12.

If the child is constipated, a small enema is given a few hours before the proposed administration, to help absorption and retention. Food is withheld for 3 hours, and $\frac{1}{150}$ or $\frac{1}{100}$ grain (0·43 or 0·65 mg.) of atropine is usually given hypodermically half an hour before the administration of thiopentone. The dose of thiopentone used is 1 g. per 50 lb. (22·7 kg.) body weight, which is dissolved in 20 to 40 ml. of warm tap-water and injected slowly into the rectum through a rubber catheter. The buttocks are then held together to prevent extrusion, but if this occurs half the initial dose is given half an hour later. The child is then allowed to lie on its side for 5 minutes. In this way complete and satisfactory sedation is obtained for examination of the fundus oculi (with 1% homatropine drops), encephalography, and other procedures not requiring surgical incisions. Opportunity is taken at the same time to palpate the liver and spleen when required. No local or general toxic effects have been observed. *E. R. Cole*

610. **The Phenomenon of Elective Thirst during Acute Dehydration in Infancy.** (Le phénomène de la soif élective au cours des déshydratations aiguës du nourrisson)
P. DEBRÉ, E. LÉVY-LOLAL, P. ROYER, A. MINKOVSKI, and S. ROYER. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 463–467, Feb. 10, 1950. 10 refs.

The authors discuss the disadvantages of various methods of replacing fluids in acutely dehydrated infants. They state that these infants fall into three classes: (*a*) those with total gastric intolerance of fluids, who must be given fluids by parenteral methods; (*b*) those

who can take fluids by mouth; and (*c*) those in whom there may be only slight vomiting or none at all, but who refuse to take fluids by mouth. Some patients in this last class may exhibit the phenomenon of " elective thirst ", in that they will drink some solutions but utterly refuse others, and this observation was applied in the treatment of 37 infants suffering from acute dehydration at the Hospital for Sick Children and the Baudelocque Hospital, Paris. The technique was simple. Each infant was offered in succession four bottles containing, respectively: (1) sodium bicarbonate, 20 g. per litre; (2) isotonic sodium chloride solution; (3) 5% glucose solution; (4) carrot soup. (Later a 2% solution of potassium lactate was also used and there are many other possibilities.)

During a one-year period (1948–49) 16 children with acute dehydration due to various causes were treated in this way, of whom 13 preferred sodium bicarbonate solution, 2 glucose, and one sodium chloride. Rehydration was successfully achieved, but 4 out of the 16 died. At the same time 21 newborn infants aged between 10 and 15 days received this treatment, together with penicillin and streptomycin, in an epidemic of severe gastro-enteritis. Of these infants 15 chose the glucose solution, 5 sodium bicarbonate, and one isotonic sodium chloride. All the infants took an effective volume of fluid by mouth, although in a few cases, because of oral infection, the solution was given by stomach tube until the mouth was free from sepsis. Of these 21 infants 3 died.

The authors point out that this phenomenon of " elective thirst " is not common, but where it does occur their method of rehydration is effective. The possibility that the infant's choice of solution may be connected with the plasma content of the ions concerned was suggested by their observations, but the whole mechanism remains obscure. The only untoward incident observed was the appearance of a subcutaneous oedema, which dispersed rapidly. *E. R. Cole*

611. **The Study of Congenital Anomalies by the Epidemiologic Method, with a Consideration of Retrolental Fibroplasia as an Acquired Anomaly of the Fetus**
T. H. INGALLS. *New England Journal of Medicine* [*New Engl. J. Med.*] **243**, 67–74, July 20, 1950. 8 figs., bibliography.

Congenital anomalies cause about 5% of all deaths in infancy. In the present paper the problem of these anomalies is attacked by the epidemiological or statistical approach. For example, it can be shown that cases of congenital blindness (due to cataract) occur most frequently when the mother contracts German measles between the first and second months of gestation (" the mean critical period for cataract is 1·17 months "); congenital deafness, on the other hand, is noted most often in the child when the mother suffers from German measles between the second and third months (" mean critical period is 2·17 months "). The difference between these means is statistically significant, and cannot be explained by regularly occurring alteration in the virulence of the virus or by changes in the external environment. The explanation is to be sought in the development of the foetus, and embryologists have pointed out that the period of active differentiation of the primary lens fibres lies between the 5th and 8th weeks, and that of the cochlea between the 7th and 10th weeks. " These observations on rubella demonstrate that the basic principles of animal teratology [the science of antenatal pathology] operate in the pathogenesis of acquired human anomalies ".

The evidence that mongolism is a stage-specific deformity due possibly to anoxia occurring between the 7th and 9th weeks of pregnancy is discussed. Congenital abnormalities, such as anencephaly, have been produced in mice, their occurrence depending on the degree of anoxia to which they are subjected and also on the stage of development of the foetus. Similarly, deficiency of riboflavin may produce cleft palate, again depending on the stage at which it is induced.

The gradient in severity of deformities is then illustrated by examples. All degrees of deformity between a two-headed monster and joined twins, between a vestigial eye and cyclopia and between cyclopia and duplicate eyes, and between complete absence of a phalanx in the hand of mongols and its presence, have been observed.

The importance of retrolental fibroplasia in the investigation of this type of problem is discussed. This condition develops in the eye of premature infants, and affords an opportunity to watch an anomaly form in the foetus. In view of the great difference in incidence of this condition as reported from different hospitals, a plea is put forward for a planned investigation on a large scale, contributions being needed from opthalmologists, obstetricians, paediatricians, pathologists, embryologists, and statisticians.

Finally " the error of assuming that an anomaly is inherited simply because it is present at birth should no longer be perpetuated ". There is now ample experimental and statistical evidence to support this.

[This is a well-written review which should be read by all those interested.] *A. T. Macqueen*

612. **A Condition Resembling the Vogt–Koyanagi Syndrome and Mandibulo-facial Dysostosis.** (Vogt–Koyanagi ähnliches Syndrom und mandibulofaciale Dysostosis)
A. LUDWIG and G. KORTING. *Archiv für Dermatologie und Syphilis* [*Arch. Derm. Syph., Wien*] **190**, 307–316, 1950. 3 figs., 32 refs.

A case history of abnormality in a boy is presented. The patient's mother had an undiagnosed febrile illness during her pregnancy and this may have been a factor in the abnormality. At birth the child showed vitiligo, especially around the scalp, and mandibulo-facial dysostosis (eyes sloping downwards, colobomata of lids, hypoplasia of maxilla and mandible, deformity of ears, high palate, and abnormal implantation of teeth and hair). At the age of 15, alopecia and poliosis and punctate white discoloration of the nails were noted. The only missing sign required to complete the Vogt–Koyanagi syndrome was uveitis; a persisting pupillary membrane was, however, taken as evidence of an intrauterine uveitis. It is thought possible that both conditions were caused by the intrauterine infection of the foetus, with or without an additional hereditary factor. *G. W. Csonka*

613. **"Three Day Fever." An Acute Febrile Disease of Childhood (Further Observations)**
C. H. WEBB and S. G. WOLFE. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **80**, 245–253, Aug., 1950. 11 refs.

This is a further study of a previously described acute febrile illness affecting 86 children. The symptoms were sudden onset of high fever with severe headache and generalized muscle pains; the infection lasted for from 2 to 4 days and was self-limited, treatment being without effect. Spread appeared to be from person to person with an incubation period of 4 to 7 days. A virus corresponding to the type-2 Coxsackie virus of Dalldorf and Sickles was isolated from 2 of the patients, and sera from 5 patients contained neutralizing antibodies against this virus. *Winston Turner*

614. **Neonatal Diarrhoea and Vomiting. Outbreaks in the Same Maternity Unit**
A. C. KIRBY, E. G. HALL, and W. COACKLEY. *Lancet* [*Lancet*] **2**, 201–207, Aug. 5, 1950. 1 fig., 34 refs.

During an outbreak of diarrhoea and vomiting in a maternity hospital in Liverpool rectal swabs were taken from infants at 7-day intervals in hospital, and at periods of from 4 to 34 days after discharge, to establish the cause. Of 144 babies at risk, 17 developed the disease while in hospital, and 13 developed it after discharge. In every case affected a profuse growth of *Bacterium coli* (var. *neapolitani*, serological type D 433) was obtained from the rectal swab. In 7 cases with positive swabs no symptoms developed, but in no case did the disease develop in an infant with a negative swab. As a control, 210 swabs from 191 infants were taken over a period of a month at a neighbouring maternity hospital. Four were positive, though none of the infants suffered from diarrhoea or vomiting. Five weeks after the end of the epidemic 9 out of 25 infants from the ward in which it had started had positive swabs, though none had symptoms.

Of the 110 infants fully breast-fed, save for the giving of glucose saline in the first 24 hours, 4·5% became ill, and 8·2% had positive swabs. Of 34 infants not directly fed at the breast (some of whom, however, received breast milk only), 67·8% became ill, and in 77·0% swabs became positive.

Symptoms varied greatly in severity. The stools were watery and usually contained mucus. Listlessness, with a marked early grey pallor not attributable to dehydration, was apparent. So long as reluctance to feed remained, there was a great tendency to relapse. This "toxic" appearance with a high incidence of relapse is almost always associated with the finding of *Bact. coli* D 433. The disease lasted from 8 to 24 days, and the mortality was 43%.

The organisms were fed to 3 adult volunteers, in whom diarrhoea and positive rectal swabs developed, though feeding of faecal *Bact. coli* and the culture media had no such effect.

A second outbreak of diarrhoea and vomiting, occurring in the same unit and affecting 16 babies, was also investigated. The clinical picture was quite different; the disease lasted on an average for 5 days, and there was no toxicity and no mortality. Of 12 rectal swabs taken all were negative for *Bact. coli* D 433.

The authors briefly discuss the aetiological significance of the organism. *H. G. Farquhar*

615. **Cardio-esophageal Relaxation. Report of Three Cases**
R. P. ALLEN. *Radiology* [*Radiology*] **55**, 214–216, Aug., 1950. 5 figs., 2 refs.

The discovery of 2 new cases of infantile vomiting caused by cardio-esophageal relaxation in the past 6 months suggests that many of the undiagnosed cases of infantile vomiting may, by proper roentgen examination, be so classified and successfully treated. Absence of intestinal gas was observed in one of these cases, a feature not previously described. When gas is absent from the intestine of an infant, cardio-esophageal relaxation must be added to the possibilities. Atropine acted favorably in a single experiment.—[Author's summary.]

616. **Interstitial Pneumonia of the Premature Infant.** (Die interstitielle Pneumonie der Frühgeburten)
E. FREUDENBERG and W. TOBLER. *Annales Paediatrici* [*Ann. paediatr., Basel*] **175**, 185–200, July–Aug., 1950. 9 figs., 16 refs.

617. **Pathogenesis of Megaloblastic Anemia in Infancy. An Interrelationship Between Pteroylglutamic Acid and Ascorbic Acid**
C. D. MAY, E. N. NELSON, C. U. LOWE, and R. J. SALMON. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **80**, 191–206, Aug., 1950. 5 figs., 33 refs.

Megaloblastic anaemia occurs in infants aged 5 to 11 months, the symptoms being uniformly insidious—increasing pallor and anorexia. Examination of the marrow is necessary for accurate diagnosis, because there may not be a macrocytosis in the peripheral blood. A lasting cure is regularly effected by folic acid. The effects of ascorbic acid, vitamin B_{12}, and pteroylglutamic acid were observed in monkeys fed on a basal milk diet similar to that of affected infants. Animals not given ascorbic acid developed megaloblastic anaemia, which was relieved by folic acid with or without the addition of ascorbic acid. Vitamin B_{12} without the ascorbic acid was not effective. The experiments indicate that a chronic deficiency of ascorbic acid leads to a secondary deficiency or failure of metabolism of folic acid or related substances, which results in megaloblastic change in the marrow. *Winston Turner*

618. **A Syndrome Resembling Progeria: a Review o Two Cases**
C. A. NEILL and M. M. DINGWALL. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **25**, 213–221, Sept., 1950. 8 figs., 16 refs.

A description is given of two brothers aged 16 and 11 years who suffered from similar physical deformities and severe mental deficiency: stature was dwarfish (the trunk being affected more than long bones), there was a definite but atypical microcephaly, lumbar lordosis, and

fixed-flexion deformity of the knees; other signs included intention tremor, unsteady gait, sexual infantilism, retinitis pigmentosa and optic atrophy, extensive intracranial calcification, impairment of sight and hearing, and gross mental deficiency.

These 2 cases resemble the cases described by Cockayne in 1936, in a brother and sister aged 6 and 7 years, under the title " dwarfism with retinal atrophy and deafness ", although there are minor differences. Cockayne did not claim any relation between his cases and progeria, but the present authors consider that there is a connexion, and give the similarities and then the differences. Among the differences are the absence in classical progeria of retinal degeneration, deafness, and intracranial calcification, and the presence of baldness and general atrophy of the skin, fairly general arteriosclerosis, and shortening of the clavicles.

They suggest, therefore, that the 2 cases they have described are due to " a multiple germ defect, similar to that of progeria, possibly caused by a recessive gene, and producing secondary extensive endocrine and metabolic disorders ". *C. McNeil*

619. **Convulsions in Childhood. An Epidemiological Note on their Association with Epilepsy, Eclampsia, and Stillbirth**

T. W. BUCHAN. *British Medical Journal* [*Brit. med. J.*] **2**, 22–23, July 1, 1950. 3 refs.

Evidence has been adduced indicating that infantile convulsions are an early manifestation of epilepsy, and it has also been suggested that they are related to certain types of convulsion in pregnancy and labour. Since eclampsia is the commonest cause of convulsion in pregnancy and labour, and is not infrequently associated with stillbirth, the author has studied the relations in incidence between infantile convulsions, epilepsy, eclampsia, and stillbirths, and points out that certain epidemiological kinships exist between them in respect of secular trend and seasonal and regional variation in England and Wales.

Mortality from these conditions is now the lowest ever, the rate for infantile convulsions (under 1 year old) having fallen from 9·68 to 0·35 per 1,000 births, and that for epilepsy (all ages) from 72 to 29 per million between 1911 and 1947, while mortality from eclampsia and the incidence of stillbirth have fallen since 1919 and 1935 respectively. It is pointed out, however, that the trend in this group is similar to that in many other diseases. Seasonal variations in mortality from these four conditions as indicated by curves of monthly mortality from 1939 to 1945 show some parallelism, all figures being maximal in the early part of the year, while mortality from infantile convulsions and from epilepsy falls to a minimum in August, and from eclampsia and stillbirth in November. Coefficients calculated from the stillbirth rates and mortality figures for epilepsy, eclampsia, and convulsions over varying periods for various geographical regions as constituted in the Registrar-General's reviews indicate a close correspondence in regional distribution, while an excess of male deaths is common to epilepsy and infantile convulsions as well as to stillbirth and neonatal mortality. A difference in the coefficients between stillbirths and mortality from infantile convulsions for the periods 1932–7 and 1939–46 is noted which, it is suggested, may be due partially to changes caused by war-time evacuation. *E. R. Cole*

620. **Hepatic Cirrhosis with Dwarfism in Early Infancy and Hypophosphataemic Rickets.** (Lebercirrhose mit frühinfantilem Zwergwuchs und hypophosphataemischer Rachitis)

A. ECKSTEIN. *Annales Paediatrici* [*Ann. paediatr., Basel*] **175**, 224–234, Sept., 1950. 6 figs., 15 refs.

Hepatic rickets, renal rickets, and the de Toni–Fanconi syndrome are grouped together as special forms of rickets not primarily caused by lack of vitamin D. In these conditions certain disturbances of liver and kidney function lead to changes in the blood chemistry producing hypophosphataemia, osteoporosis, dwarfism, " glycolability ", albuminuria, and acidosis. They have the further common characteristic of being refractory to treatment with vitamin D, even in the highest doses.

A case of a new form of hepatogenous rickets is described in a boy of 12 years of age. The disease started at the age of 4 with anorexia, pallor, slight jaundice, and increasing weakness. There was evidence of severe liver cirrhosis and active rickets which persisted in spite of treatment with vitamin D. The leading clinical signs were marked dwarfism with severe rachitic deformities of the head, chest, limbs, and spine. The abdomen was grossly distended and the liver and spleen were moderately enlarged. The *x*-ray examination of the skeleton revealed widespread osteoporosis of the long bones, ribs, and pelvis, with active rickety changes in the epiphysial lines and fresh greenstick fractures of the arm bones which had occurred spontaneously during the vitamin-D therapy. There was also a marked hyperossification of the skull bones. No signs were found of kidney damage or disturbances of glycogen metabolism. The urine was free from sugar, albumin, and bilirubin, the concentration and dilution tests were normal, but the test for urobilinogen was strongly positive. There was a non-haemolytic, hyperchromic anaemia, with a normal bone-marrow picture. Blood chemistry and liver function tests confirmed the clinical findings of active rickets and severe hepatic damage, the serum content of phosphorus being 2·9 mg. per 100 ml., of calcium 11·8 mg. per 100 ml., and of alkaline phosphatase 20·2 Bodansky units, the van den Bergh reaction indirectly positive, thymol-turbidity reaction 10 units, and Takata–Ara reaction strongly positive. There was a slight acidosis with an alkali reserve of 42 volumes of CO_2%. Treatment with high doses of vitamin D (1,500,000 i.u. in 20 days, 600,000 of which were administered intramuscularly) was ineffective. The causative relation between cirrhosis of the liver and severe rickets is not regarded as firmly established. Though cases of congenital atresia of the bile duct with acholia are frequently complicated by severe osteoporosis and hypophosphataemia, in many cases of cirrhosis no rickety changes develop. It therefore seems more accurate to define the condition as hypophosphataemic osteoporosis. Further studies are required to clarify its pathogenesis.

M. Dynski-Klein

Medicine: General

621. **The Rôle of the Cerebral Cortex in the Apperception of Pain**
G. W. THEOBALD. *Lancet* [*Lancet*] **2**, 41–47, July 9, 1949. 5 figs.

In this paper the author records the first part of his clinical observations on visceral pain and its relief by anaesthetizing the area to which it is referred. The vaginal mucosa above the level of insertion of the hymen was found to be one of the most insensitive structures in the body, except to galvanic and faradic currents. During operations under local analgesia in the lower abdominal cavity without premedication, extraperitoneal tissue was always found to be sensitive and parietal peritoneum fairly insensitive. The body of the uterus was comparatively insensitive and could be incised without causing pain. The Fallopian tubes were invariably extremely sensitive, and rough handling of them caused so much pain that every structure became hypersensitive. The ovaries were practically insensitive.

In healthy women the fundus and cervix of the uterus were stimulated with faradic current by means of electrodes of special form. Pain was in each case referred to an area in the midline of the abdomen and $1\frac{1}{2}$ in. (3·75 cm.) above the upper border of the symphysis pubis. As the intensity of stimulation and the pain resulting increased, so did the area of reference. Mild pain was relieved by intradermal injection of saline, more severe pain by procaine solution. Neither solution was effective against the severest pain. It is suggested that the quantitative data support the author's view that referred pain is appreciated by the summation of stimuli from the viscus concerned and the cutaneous area of reference.

It was suggested to a subject under hypnosis that a skin area touched with a pencil would be painful; this area was subsequently surrounded by an area of cutaneous hyperalgesia for some hours. It is suggested that this phenomenon is of cortical origin. Clinical observations are quoted in support of the view that referred pain is often localized with precision, but the site of reference may be unpredictable. *R. A. Gregory*

622. **Observations on the Structure of Clubbed Fingers**
R. R. H. LOVELL. *Clinical Science* [*Clin. Sci.*] **9**, 299–321, 1950. 7 figs., 20 refs.

In the first part of this paper from St. Mary's Hospital, London, the author analyses the differences between normal and clubbed fingers in the living, and describes the change brought about in the volume of the distal segment of each by compression with a rubber bandage, which was regarded as an index of the volume of blood contained. In the second part he describes a study of the vascular system in post-mortem specimens of clubbed fingers by means of intravascular staining and "neoprene" injections. Fourteen normal fingers, 10 clubbed fingers associated with bronchopulmonary disease, and 8 clubbed fingers associated with congenital heart disease were investigated in the living. The post-mortem material consisted of 2 normal fingers, one finger from a subject with congenital heart disease, and 4 from subjects with bronchopulmonary disease.

It is concluded from these investigations that the essential change in clubbing of the fingers is an increase in the connective tissue of the distal finger segment, and that this is maximal between the nail and the dorsum of the distal phalanx. An increase in calibre of the branches of the digital arteries is also demonstrable in clubbed fingers. In cases of congenital heart disease, but not in cases of bronchopulmonary disease with clubbing, there is, in addition, an increase in the volume of blood in this segment, due to dilatation of the venous plexuses of the skin and the nail bed, possibly associated with the increase in total blood volume. The author considers that failure to make this distinction between clubbing of the fingers due to congenital heart disease and that associated with other diseases accounts for the confusion which has arisen about the nature of the structural changes. It is suggested that the increase in connective tissue is secondary to an increased blood flow in excess of local physiological needs—"forced feeding"—which may in turn be due to a local predominance of arteriovenous anastomoses. *A. T. Macqueen*

ALLERGIC DISORDERS

623. **Precipitin Reaction in the Diagnosis of Allergic Patients**
C. JIMÉNEZ DIAZ, E. ARJONA, J. M. ALES, and J. M. SEGOVIA. *Annals of Allergy* [*Ann. Allergy*] **8**, 496–507, July–Aug., 1950. 19 refs.

A "micro-precipitin" reaction was studied, based upon the adsorption of antigen on collodion particles. The authors believe that the "micro-precipitin" bears no relation to other antibodies involved in allergy—the micro-precipitin present in anaphylaxis and major allergies, the reagins demonstrated in hay-fever and allied allergies, and the blocking antibodies in hay-fever after treatment.

Goodner's simplified procedure of Zozaga's technique was used (*Science*, 1941, **94**, 242). Blood was taken from fasting subjects, menstruating females being excluded, and the serum was used fresh. The antigen solution contained 1 mg. of protein in 10 ml. of saline and the *p*H was adjusted to 7·8.

The precipitin reaction was studied in 120 subjects with no known allergic disease, the commonest food allergens being used. Only in 14 cases (11·6%) were positive results obtained. Thirty-four non-allergic persons were tested for precipitins against the common airborne fungi; no precipitin was found. In contrast, sera of asthmatic patients gave positive precipitin reactions. The highest

figures (40·9%) were obtained in the group of cases with asthma and negative skin reactions, termed by Coca "cases of familial non-reaginic food allergy". Sera of patients sensitive to fungi gave positive precipitin reactions in 36% of cases. The diagnosis of sensitivity was based on the history and not on the skin tests. The latter were often negative. In pollinosis only reagins were found and no micro-precipitins. Sera from patients suffering from hay-fever and undergoing pollen desensitization were examined for blocking antibodies and for micro-precipitins. Whereas the titre of the blocking antibodies rose steadily, no micro-precipitins were observed. *Kate Maunsell*

624. **The Problem of Aspirin Allergy with a Report on Skin Testing with Salicylate-containing Human Sera**
K. P. MATHEWS, R. G. LOVELL, and J. M. SHELDON. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 416–421, Sept., 1950. 19 refs.

It is well known that skin tests by the scratch, intradermal, patch, and passive transfer methods are rarely positive in aspirin-sensitive individuals. Because of this, and because administration of a test dose of aspirin may be dangerous, the authors sought some alternative form of test for aspirin sensitivity. The following methods were employed:

(1) The serum of patients receiving aspirin (mainly for rheumatic fever and rheumatoid arthritis) was used as testing material. The salicylate level in the test sera varied between 6 and 24 mg. per 100 ml. Each of 12 aspirin-sensitive patients was tested with the salicylate-containing serum, normal serum, and sterile saline by both the prick and intradermal methods, and 6 of these patients were tested with salicylate-containing sera from two sources. All sera used were also tested in a normal individual. In none of the aspirin-sensitive patients was there an appreciable difference in effect between the salicylate-containing serum and the control serum—both caused a moderate degree of whealing in many patients when administered intradermally. (2) Rheumatic patients receiving aspirin were injected intradermally with serum from aspirin-sensitive patients. In no case did a significant reaction develop at the site of injection. (3) Serum from 6 aspirin-sensitive patients was injected intradermally into the skin of a known passive-transfer receptor. After 48 hours the sites were tested with salicylate-containing serum, control serum, a 1 in 300 solution of aspirin in saline, and sterile saline, by both prick and intradermal methods; all prick tests were entirely negative and there was no difference between the whealing produced with salicylate-containing serum and control serum given intradermally. (4) A suitable subject was injected with salicylate-containing serum, control serum, 1 in 300 aspirin solution in saline, and sterile saline. These sites were tested by both prick and intradermal methods with serum from 6 aspirin-sensitive patients, normal serum, 1 in 300 aspirin solution in saline, and saline. Again the results were negative.

All tests were read after 20 minutes, 24 hours, and 48 hours. The authors conclude that the clinical history is, at present, the only satisfactory means of diagnosing aspirin allergy. *R. S. Bruce Pearson*

M—M

625. **Standardization of Dust Extracts. 1. Standardization on the Basis of Equal Molecular Size**
M. SCHERAGO, B. BERKOWITZ, and M. REITMAN. *Annals of Allergy* [*Ann. Allergy*] **8**, 437–452, July–Aug., 1950. 2 figs., 5 refs.

Six house dust extracts were prepared, analysed for total nitrogen and for phosphotungstic acid nitrogen by the methods of Rockwell, Thomas and Wittich, and tested for skin potency by the intradermal injection of persons sensitive to house dust. In confirmation of their findings and of those of others, no correlation was found between the skin potencies of the extracts and their total nitrogen or phosphotungstic acid-precipitated nitrogen content.

The six extracts were found to be approximately equal in molecular size. When they were diluted to the same phosphotungstic acid nitrogen content and tested for skin potency by the intradermal injection of persons sensitive to house dust they failed to elicit skin reactions of the same magnitude. This finding is in contrast to the findings of Rockwell *et al.* Since the active substance responsible for the allergenic potency of dust extracts is not known, methods of standardization that are based on determinations of nitrogen in any form cannot be depended upon to yield reliable information concerning the allergenic potency of these extracts. The certification of allergenic extracts on the basis of a method of standardizing that requires the use of human volunteers for skin testing is not feasible.—[Authors' summary.]

626. **Standardization of Dust Extracts. II. *In vitro* Leukocytolysis in the Assay of the Allergenicity of Dust Extracts**
B. BERKOWITZ and M. SCHERAGO. *Annals of Allergy* [*Ann. Allergy*] **8**, 453–467, July–Aug., 1950. 7 refs.

[This paper is of greater theoretical than practical interest.] Squier and Lee (*J. Allergy*, 1947, **18**, 156) reported that heparinized blood from a ragweed-sensitive patient when incubated with ragweed antigen caused lysis of leucocytes, approximately in proportion to the degree of sensitivity of the patient. In the present work sensitized rabbit leucocytes were tested against allergens and leucocytolysis was observed. Four rabbits were injected with dust antigen, and 21 days after the last injection their heparinized blood was tested against serial dilutions of dust antigen. As controls blood–saline mixtures were made, and a parallel arrangement was examined, with blood from normal rabbits. The leucocyte count decreased in the mixtures containing sensitive blood and dust antigen, but leucocytolysis was not strictly proportional to the increasing concentrations of the dust antigen.

In a second test, blood from normal rabbits was sensitized passively *in vitro* with serum from sensitized rabbits, and later incubated with dust antigen in varying concentrations. Leucocytolysis was observed, but again no constant figures were obtained. A third set of experiments dealt with the comparison of various samples of dust as regards their leucocytolytic and skin-reacting properties. Intensities of leucocytolysis and skin reaction were not always parallel. *Kate Maunsell*

627. **A Clinicopathologic Study of Bronchial Asthma with Consideration of its Relationship to the " General Adaptation Syndrome "**
B. M. WINER, J. F. BEAKEY, and M. S. SEGAL. *Annals of Internal Medicine* [*Ann. intern. Med.*] **33**, 134–162, July, 1950. 5 figs., 37 refs.

Of 46 post-mortem records consulted, roughly one-third were of patients who died in an attack of, and because of, asthma, one-third were of sufferers from asthma who had died from one or other of its complications, and one-third were of asthmatics who had died from intercurrent or unrelated disease.

To a varying extent all the patients with asthma showed changes in the lymphoid and endocrine tissues consistent with reaction to stress and consistent with more or less successful adaptation to it. The histological changes were consistent with reaction to histamine, alarm, adrenaline, and anoxia. The changes were most marked in those who died of an attack of asthma and progressively less prominent in the other two groups.

[This is a modest article, probably the forerunner of many, designed to show that asthma falls into the class of maladies associated with adaptation to stress and strain.] *G. F. Walker*

628. **Treatment of Status Asthmaticus with Nitrogen Mustards.** (Primeros resultados del tratamiento del asma pertinaz con las mostazas nitrogenadas)
C. JIMÉNEZ DÍAZ, J. PERIANES, A. MERCHANTE, C. LAHOZ, V. BARRANTES, and F. LAHOZ. *Revista Clínica Española* [*Rev. clín. esp.*] **38**, 122–123, July 31, 1950. 8 refs.

The authors note that nitrogen mustard has an anti-mitotic effect, and causes changes in the blood and lymphoid tissue similar to those produced by adreno-corticotrophin. They have consequently tried the effect of nitrogen mustard in cases of rheumatoid arthritis and asthma. Of six cases of asthma so treated, one showed great improvement, and asthma disappeared completely in the other five after the second day of treatment. The blood eosinophil count was also considerably diminished. No details of dosage are given. *René Méndez*

629. **The Endobronchial Treatment of Asthma.** (Die endobronchiale Behandlung des Asthma bronchiale)
W. SCHNEIDER. *Therapie der Gegenwart* [*Ther. d. Gegenw.*] **89**, 301–304, Sept., 1950. 13 refs.

630. **Allergic Reactions from the Ingestion or Intravenous Injection of Cane Sugar (Sucrose)**
T. G. RANDOLPH and J. R. ROLLINS. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 242–248, Aug., 1950. 13 refs.

631. **Newer Antihistaminics: III. Some Pharmacologic and Therapeutic Effects of β-(*p*-Methylbenzhydryloxy)-ethyldimethylamine Hydrochloride, a Derivative of Diphenhydramine Hydrochloride**
T. H. MCGAVACK, A. M. SHEARMAN, J. WEISSBERG, A. M. FUCHS, P. M. SCHULMAN, J. CHEVALLEY, I. J. DREKTER, and L. J. BOYD. *Journal of Allergy* [*J. Allergy*] **21**, 353–370, July, 1950. 2 figs., 25 refs.

METABOLIC DISORDERS

632. **Massive Transfusion of Serum in Protein Deficiency.** (Массивные переливания сыворотки при белковой недостаточности)
P. M. AL'PERIN and V. V. VINOGRADOV. Терапевтический Архив [*Terap. Arkh.*] **22**, No. 4, 54–58, July-Aug., 1950. 3 figs.

In liver disease, nephrosis, severe suppuration, and disease of the intestine the serum protein values may fall to abnormal levels. Seven patients with serum protein levels of 4·2 to 6·9 g. per 100 ml. were each given 3·1 to 5·2 litres of serum by drip transfusion in 7 to 9 doses over periods of 10 to 30 days. Five of the patients had oedema and in 4 of these the oedema disappeared, while it diminished in the fifth. This fifth patient, who had had the highest average daily dose of serum, had 4 reactions, 2 allergic and 2 febrile. No such reactions occurred in any of the other cases. The 5 patients with oedema excreted rather less diurnal urine after treatment. In the 7 patients the serum protein level was raised by 0·3 to 2·4 g. per 100 ml. *Jeffrey Boss*

633. **Signs of Malnutrition in Canada**
L. B. PETT. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **63**, 1–10, July, 1950. 24 figs., 2 refs.

634. **Acute Idiopathic Porphyria. Report of Two Cases**
D. W. ASHBY and E. BULMER. *British Medical Journal* [*Brit. med. J.*] **2**, 248–251, July 29, 1950. 2 figs., 26 refs.

The first of 2 cases of idiopathic porphyria described is that of a woman of 51 years, with a 6 weeks' history of central abdominal pain, aching in the limbs, fatigue, and insomnia. Three weeks after onset the urine had become dark red in colour. When first seen she was drowsy, disorientated, and confused. The conjunctivae were injected and the skin showed brown pigmentation. There was then no other abnormality in the nervous system, but 2 days later extensive weakness of lower motor neurone type developed in all the limbs and the trunk. Bilateral facial weakness gave the patient a myasthenic appearance. She was unable to lift either head or limbs from the bed. Though she complained of numbness, sensation was objectively unimpaired. The urine was dark red in colour and the absorption bands of porphyrin were seen. Total output of urinary porphyrin was measured by fluorometric comparison with a standard porphyrin solution, and fluctuated widely between 150 and 850 μg. per day. The presence of porphyrin could not be detected spectroscopically in the serum. There was no excessive sensitivity to an erythema dose of ultraviolet light. Serum potassium level was normal. Nicotinic acid, aneurin, neostigmine, and quinine were all without effect on the condition. After a month muscle power gradually returned, till she was able to walk unaided. A year later porphyria was absent, but there was residual weakness in the extensors of the legs and right wrist.

The second patient was a woman, aged 74, believed to be the oldest recorded sufferer from the condition.

Passage of red urine was followed by visual hallucinations. A blood pressure of 220/120 mm. Hg was the only other abnormality. Fourteen weeks later lower abdominal pain and vomiting developed and she became increasingly weak until unable to move her arms or legs. There ensued retention of urine. An almost complete flaccid paralysis of arms and legs was then present. She was catheterized, and the urine obtained was burgundy-coloured, containing 2·1 mg. of coproporphyrin per litre and 103·9 mg. of uroporphyrin per litre. She died on the following day.

The authors review briefly the aetiology, pathology, symptomatology, and diagnosis. A useful series of references relating to this rare condition is given. Diagnosis has to be made from other types of ascending motor paralysis, from diphtheria, lead poisoning, and botulism, and from the symptomatic porphyria due to sulphonal or methylsulphonal. *C. L. Cope*

635. **A Clinical Study of Pellagra.** (Estudo clínico da pelagra)
C. COUTO. *O Hospital* [*Hospital, Rio de J.*] **38**, 1–52, July, 1950. 10 figs., bibliography.

This is a comprehensive article describing 15 cases of pellagra. The author describes the history of the disease and deals with all the known aetiological factors. Pellagra was considered an infectious disease until Wilson cured cases by high-protein diet and Goldberger carried out his classical studies on nicotinic acid. The author mentions the endemic form of pellagra, always related to poverty and poor nutrition, and the sporadic variety, related to chronic alcoholism and other morbid gastro-intestinal conditions. Flinter, in Rumania, found that achylia gastrica was common in his cases, and it has also been noted that pellagra may follow resection of a part of the gastro-intestinal tract or amoebic dysentery. There is the possibility that maize, a basic food in many countries, contains an active anti-nicotinic-acid principle. Importance is also attached to the lack of tryptophan, which may be a precursor of nicotinic acid; there is almost certainly a coincident lack of adermin, pantothenic acid, and riboflavin. The author quotes Sydenstricker, an authority on the subject, who states that pellagra is almost certainly due to lack of several vitamins and not solely nicotinic acid.

All the patients described suffered from severe malnutrition, especially as regards animal proteins, and many were chronic alcoholics. The basic diet was one of black beans and rice. The serum protein level was nearly always low and there was inversion of the albumin–globulin ratio. The author does not tabulate the incidence of signs and symptoms, but nearly all the cases presented with one of the classical symptoms such as diarrhoea or skin lesions. Abdominal pain was very frequent, and there was also abdominal tenderness. A general erythema of the extremities was followed by the formation of bullae, which became secondarily infected. The legs were nearly always oedematous and the face was sometimes swollen. The tongue was frequently red and glazed. Diarrhoea and vomiting were almost universal. Some of the patients complained of marked dyspnoea on exertion. One patient was unable to give a reasonable history because of mental confusion, and another was demented, with delusions. Pain in the extremities was common, especially on walking, and the deep reflexes were mostly absent.

The author believes that pellagra is common in Brazil and that the diagnosis is frequently missed. He also supports the concept of " pellagra sine pellagra ". [It is a pity that he does not attempt to analyse the symptoms and signs more fully, instead of quoting the opinions of innumerable authorities on the disease.]

Paul B. Woolley

636. **The Effect of Salicylates and Adrenocorticotropic Hormone upon the Miscible Pool of Uric Acid in Gout**
J. D. BENEDICT, P. H. FORSHAM, M. ROCHE, S. SOLOWAY, and DEW. STETTEN. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1104–1111, Aug., 1950. 6 figs., 13 refs.

The magnitude of the " miscible pool " of uric acid in a patient suffering from severe chronic tophaceous gout has been determined by measurement of the dilution of isotope which occurred when uric acid labelled with N^{15} was injected intravenously. This pool, which increased to a value of about 31 g., or about 30 times normal, fell to a value of about 2 g., or approximately twice normal when the uricosuric doses of acetylsalicylic acid were given.

The effect of ACTH upon uric acid metabolism has been studied in both gouty and the normal male subjects. The resultant uricosuria appears to arise exclusively from an increased renal clearance of uric acid. Colchicine had no demonstrable effect upon the quantities measured.

It has proved feasible to divide miscible uric acid into three compartments: (1) in solution in plasma water; (2) in solution in non-plasma body water; (3) in the solid phase. It is predominantly the uric acid in the last of these compartments that is subject to wide excursions in response to therapy.—[Authors' summary.]

DIABETES

637. **The Mechanism of Glycosuric Diuresis in Diabetic Man.**
W. A. BRODSKY, S. RAPOPORT, and C. D. WEST. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1021–1032, Aug., 1950. 6 figs., 32 refs.

The mechanism of diuresis was studied in 3 young men suffering from diabetes with glycosuria, but no acidosis. Food and drink were withheld for 16 hours and then glucose, mannitol, or urea was administered by mouth or vein. The urine flow was found to be determined by the total amount of solutes in the urine rather than by the quantity of any single constituent. Thus the mechanism is the same as in non-diabetic subjects and does not depend on any specific effect of glucose. Losses of sodium and chloride increased sharply during diuresis in almost direct proportion to the rate of urine flow. Potassium and phosphate losses increased only to a small extent with increases in urine flow. *K. Black*

638. **Time Action of Globin Insulin Compared with That of Protamine Insulin Modifications**
A. R. COLWELL, J. H. ROHR, and B. B. REEB. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 178–188, Aug., 1950. 2 figs., bibliography.

This article from the Northwestern University Medical School, Chicago, represents an attempt to evaluate the present-day position of the " intermediate " insulins. These insulins consist of three main types: (1) protamine zinc and soluble insulin mixtures; (2) globin insulin with zinc; (3) crystalline protamine insulin. The authors point out that the most commonly used intermediate insulin in America is a 2 to 1 mixture of soluble insulin and protamine zinc insulin, both in 80-unit-per-ml. strength, mixed thoroughly in the syringe. Crystalline protamine insulin, or " NPH 50 ", was prepared in Hagedorn's laboratory and contains about 40% as much protamine as the commercial preparations. It can therefore be considered similar in action to the above-mentioned 2 : 1 mixture, and has the advantage that it is constant in protamine content.

The authors compared the actions of three intermediate insulins with those of soluble and protamine zinc insulin in 2 patients with diabetes of moderate severity. One single large dose (60 units) was given hypodermically and meals of similar calorific value were given every 4 hours. Levels of sugar in blood and urine were determined every 4 hours until they became relatively constant. All three types of " intermediate " insulin were similar in time action. All three insulins exerted their strongest effect in 8 to 16 hours and gradually became less effective thereafter. The authors admit that the time relationship of the curves in the 2 cases would not hold for all grades of severity of diabetes. They suggest that the difference in clinical effects of the intermediate insulins is negligible and that most cases of severe diabetes can be managed well by the use of one of this group, with the addition in some cases of soluble insulin.

I. McLean-Baird

639. **Protection against Diabetes with Nicotinamide**
A. LAZAROW, J. LIAMBIES, and A. J. TAUSCH. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 249–258, Aug., 1950. 39 refs.

The intravenous injection of 40 mg. of alloxan per kg. body weight into 28 well-fed male rats induced diabetes, recognized by a blood sugar concentration of more than 150 mg. per 100 ml. after 48 hours in 25 (89%) of them. When this dose was preceded, 1 minute earlier, by an intravenous injection of 7·5 mM of nicotinamide per kg., 12 out of 35 rats (34%) developed diabetes, indicating a significant degree of protection. On the other hand, a dose of 2·5 mM of nicotinamide per kg. given 1 minute before the alloxan had no significant protective effect, 14 out of 19 rats (74%) developing diabetes, whereas when the same dose was injected 60 minutes before the alloxan it exerted a marked protective effect, only 4 out of 27 rats (15%) becoming diabetic. The protective effect of nicotinic acid was similar to that of nicotinamide, a dose of 2·5 mM per kg. being effective only when given 60 minutes before the alloxan. Of the two, nicotinamide (8 diabetic rats out of 23 injected) was more effective, on a " mol-for-mol " basis, than nicotinic acid (15 diabetic out of 26). Ways in which nicotinamide exerts its protective effect are discussed. *M. Lubran*

640. **The Significance of Conjunctival Aneurysms in Diabetics**
C. MCCULLOCH and T. J. PASHBY. *British Journal of Ophthalmology* [*Brit. J. Ophthal.*] **34**, 495–505, Aug., 1950. 9 figs., 11 refs.

Diabetic aneurysms have already been described in the retina and may also occur in the kidney. While looking for aneurysms in other tissues, the authors found conjunctival aneurysms in 55% of diabetics and 14% of normal persons. Among diabetic patients, rather more aneurysms occurred in those with retinopathy than in those without it.

The aneurysms were seen on the bulbar conjunctiva and were of the berry type, with or without a visible vessel, purple in colour, with sharp borders and smooth surfaces. There were often accompanying areas of haemorrhage and dilated tortuous veins. Other clinical investigations made in an attempt to differentiate cases with aneurysms from those without, including tests of capillary fragility, gave negative results.

The authors suggest that the circulation to the middle layers of the retina, the glomeruli of the kidney, and the islets of Langerhans of the pancreas is similar. They also suggest that in diabetic patients hyaline changes occur in the capillary walls in all three situations, and that the varying degree of these changes determines the severity of the diabetes, renal damage, and retinopathy in any one case. *C. A. Brown*

641. **Hepatic Insufficiency and Cirrhosis in Diabetes Mellitus**
J. J. FRANKEL, C. E. ASBURY, and L. A. BAKER. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 376–390, Sept., 1950. Bibliography.

A great many myths about diabetes mellitus, and especially about hepatic function in that disease, are copied from textbook to textbook. The authors studied 139 diabetic patients, and by a whole " profile " of tests of hepatic function in each case found defective function of the liver in 46. Of these 46, however, only 18 could be shown to have a disorder of liver due solely to diabetes mellitus. In the remainder other factors, such as heart disease and alcoholism, were present. In a later series the authors studied 36 patients who suffered from both diabetes mellitus and cirrhosis of the liver. Of these only one could be proved to have cirrhosis of the liver solely as a result of diabetes.

Liver enlargement with fatty infiltration as a phase of diabetes mellitus is much over-emphasized in textbooks; it is in fact quite uncommon in adults, though possibly not so uncommon in children. Gross liver disease tends to disorder of glucose tolerance and may lead to hypoglycaemia. Diabetes mellitus may quite frequently lead to a temporary and transient disorder of hepatic function, but it does not often cause permanent damage to the liver. *G. F. Walker*

Cardiovascular Disorders

642. **Unipolar Electrocardiographic Studies in Congenital Heart Disease in Infancy**
A. I. SCHAFFER. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **80**, 260–267, Aug., 1950. 6 figs., 13 refs.

The author describes unipolar electrocardiograms of 5 infants with congenital heart lesions, each of which was confirmed at necropsy. In 4 cases abnormal ventricular preponderance was diagnosed, on the evidence of leads V6r and/or V4r and aVL. Left ventricular preponderance is always abnormal at this age, but it is impossible to distinguish between normal and abnormal right ventricular preponderance unless serial tracings are taken. In one baby with interauricular and interventricular septal defects and a dextroposed aorta the electrocardiogram showed a transitory pattern of endocardial injury, in the form of a raised S–T interval when crying, perhaps indicating reduced coronary blood flow.
Winston Turner

643. **The Normal Electrical Axis or Left Axis Deviation in Morbus Coeruleus. Study of 29 Cases. Diagnostic Significance.** (L'axe électrique normal ou dévié à gauche dans les cardiopathies congénitales cyanogènes. Étude de 29 cas personnels—intérêt diagnostique)
E. DONZELOT, M. DURAND, C. METIANU, and P. VLAD. *Archives des Maladies du Cœur et des Vaisseaux* [*Arch. Mal. Cœur*] **43**, 577–598, July, 1950. 13 figs., 28 refs.

Among 527 patients with congenital heart disease of the cyanotic type treated at the centre for cardiovascular disorders at the Broussais Hospital, Paris, 29 did not show the usually associated right electrical-axis deviation. The electrocardiogram in 22 showed left axis deviation, and in the remaining 7 the electrical axis was normal. The former group comprised 18 patients with tricuspid atresia, 1 patient with coarctation of the aorta (infantile type), 1 with partial transposition of vessels, pulmonary stenosis, and ventricular abnormalities not well defined, and 2 others with an uncertain diagnosis. The latter group of 7 was composed of 3 cases of tricuspid atresia, 1 case of Eisenmenger syndrome, 1 case of tetralogy of Fallot with persistence of the ductus arteriosus, 1 case of tetralogy of Fallot with interauricular communication, and 1 case of pulmonary haemangioma. The ages of the 29 patients ranged from 12 months to 19 years.

The electrocardiographic study of the above cases, as well as a study of the literature on the subject, have shown that the electrical axis is rarely normal in Fallot's tetralogy and in Eisenmenger's complex. In the few instances where such a normal axis is found, it should be concluded that an added cardiac lesion or malformation exists. A normal axis in a case of tricuspid atresia must mean that some degree of left ventricular hypertrophy is present. On the other hand, the finding of left axis deviation in cyanotic heart disease is also a rare phenomenon; its significance is quite clear. Thus its demonstration in a case of Fallot's tetralogy excludes this simple diagnosis, for it is almost certain that added cardiac lesions are present. Eisenmenger's complex is never associated with left axis deviation. In conclusion, when left axis deviation is present in a case of congenital heart disease with cyanosis, two conditions come to mind immediately: tricuspid atresia and the much rarer condition of coarctation of the aorta of the infantile type (in children after the age of 2 or 3).
A. I. Suchett-Kaye

644. **Normal Unipolar Variants with Special Reference to the Q and T Waves**
P. C. GAZES. *American Heart Journal* [*Amer. Heart J.*] **40**, 30–46, July, 1950. 10 figs., 13 refs.

645. **The Q Wave in Esophageal Electrocardiography**
A. A. SANDBERG, L. SCHERLIS, A. GRISHMAN, A. M. MASTER, and J. WENER. *American Heart Journal* [*Amer. Heart J.*] **40**, 47–52, July, 1950. 3 figs., 17 refs.

646 **The Comparative Value of the Augmented Unipolar Limb Leads versus the Standard Limb Leads in Myocardial Infarction**
D. FISKE. *American Heart Journal* [*Amer. Heart J.*] **40**, 53–62, July, 1950. 1 fig., 4 refs.

647. **Acute Primary Pericarditis**
I. A. FEDER, J. HOFFMAN, and H. SUGAR. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220**, 144–155, Aug., 1950. 11 figs., 16 refs.

Acute primary pericarditis is believed by the authors to be more common than is generally recognized. Five illustrative cases are described. The chief complaint was of substernal or precordial pain, often during a respiratory infection. Clinical signs of a pericardial effusion and pleural effusion were sometimes found. Serial electrocardiograms showed elevation of the RS–T segment and inversion of the T wave. In some cases the electrocardiographic signs persisted after the symptoms had disappeared. Radiological examination showed a typical change in cardiac silhouette. The condition may recur. No definite aetiological factor has been found and the treatment is symptomatic. The relation of the condition to constrictive pericarditis has not been determined.
H. E. Holling

648. **Chronic Obstruction of Major Pulmonary Arteries**
D. CARROLL. *American Journal of Medicine* [*Amer. J. Med.*] **9**, 175–185, Aug., 1950. 3 figs., 13 refs.

Case histories of 5 patients with chronic pulmonary artery obstruction are given in full; 4 patients came to necropsy and the diagnosis was verified by biopsy examination in the remaining case. The difficulty of

making the diagnosis is emphasized, but it was found that a diagnosis of chronic pulmonary artery obstruction could always be considered when there were cyanosis and right-sided cardiac failure without any other obvious cause.

Radiography and angiocardiography in one case revealed absence of vascular marking in one lung field. This evidence was useful in establishing a diagnosis.

J. B. Wilson

649. **Influence of Arterial Disease on the Systolic Blood Pressure Gradients of the Extremity**

T. WINDSOR. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220**, 117–126, Aug., 1950. 9 figs., 5 refs.

Systolic blood pressure was estimated at different levels in the limbs of resting normal subjects and patients with peripheral vascular disease by noting the pressure in an occluding cuff at which pulsation appeared in a digital plethysmograph. The systolic pressure readings obtained agreed well with those found by auscultation [but were not compared with intra-arterial measurements].

In normal subjects the pressure gradient was higher in the lower limb than the upper. In cases of peripheral vascular disease the systolic pressure was found to be diminished distal to an obstruction; the results of application of the occluding cuff at several levels in a limb gave some indication of the site of obstruction.

D. Verel

HEART

650. **Prophylaxis of Recurrent Embolism of Intracardiac Origin. Protracted Anticoagulant Therapy on an Ambulatory Basis**

S. W. COSGRIFF. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 870–872, July 8, 1950. 27 refs.

This paper from the Presbyterian Hospital, New York, records the continuous treatment with dicoumarol of 17 patients with recent embolic complications of cardiac origin, the majority having rheumatic heart disease and auricular fibrillation. The duration of this ambulant treatment varied from 3 to 27 months, 10 patients receiving treatment for 12 months or longer. After initial stabilization, prothrombin time was estimated once a week. In no instance was serious bleeding encountered.

The author discusses the problems of determination of the optimum period of treatment and of the assessment of results. From a comparison of the previous history of recurrent embolism in his patients with their condition during and after treatment, he concludes that "a favourable effect was produced". In 15 cases the clinical course during treatment was uneventful, while 2 patients suffered embolism, one pulmonary and the other renal, while under treatment. One patient had a fatal cerebral embolism, and 2 others developed non-fatal embolism, after dicoumarol was stopped.

R. N. Johnston

651. **Thyrotoxic Heart Disease. Study of 150 Cases. II. Clinical Forms, Evolution, and Treatment.** (La cardiopatía tirotóxica: estudio de 150 casos. II. Formas clinicas, evolucion y tratamiento)

J. ORTIZ VÁZQUEZ, A. DUQUE SAMPAYO, and P. PÉREZ GONZÁLEZ. *Revista Española de Cardiologia* [*Rev. esp. Cardiol.*] **4**, 316–348, July–Aug., 1950. 5 figs., bibliography.

A series of 150 patients with thyrotoxic heart disease were placed in the following groups: (*a*) common type of cardiac irritability and insufficiency, 62; (*b*) cardiac irritability, 41; (*c*) thyrotoxic cardiac insufficiency, 22; (*d*) thyrotoxic coronary insufficiency, 7; (*e*) thyrotoxic arrhythmias, 18.

In 99 cases thyrotoxicosis was the only aetiological agent, and in 51 cases the thyrotoxic state was complicated—by a rheumatic factor in 13, a hypertensive factor in 12, and an arteriosclerotic factor in 26.

In group (*a*) the patients had symptoms of cardiac irritability plus insufficiency. Clinically there was a cardiac enlargement, confined to the pulmonary arc, left auricle, and left ventricle.

In group (*b*) the subjective symptoms were added to those of a neurocirculatory asthenia [though it is difficult to see how the subjective symptoms of thyrotoxic cardiac irritability and those of the neurocirculatory state could be dissociated, except by the presence or otherwise of a toxic goitre]. This irritable state is in many cases the antecedent of the other clinical syndromes. It is generally found in younger patients and treatment is as a rule very efficacious.

Cardiac insufficiency in thyrotoxicosis (group (*c*)) differs from insufficiency in general in the less frequent occurrence of cyanosis, the more rapid circulatory rate in the presence of failure, and the infrequency of gallop rhythm and paroxysmal dyspnoea.

Group (*d*) was characterized by the presence of anginal pain. Patients tended to be older (over 40 years) and the arteriosclerotic factor could not be ignored. The changes in rhythm produced by thyrotoxicosis (group (*e*)) may be paroxysmal, transitory, or permanent. The most common form of arrhythmia was auricular fibrillation.

The association of thyrotoxic heart disease and rheumatic fever is discussed. The difficulty in diagnosis is stressed. In rheumatic fever thyrotoxic symptoms occur relatively frequently. It is probable that both rheumatic fever and thyrotoxicosis find a fertile ground in the irritable and asthenic constitution of these patients. Hypertension and arteriosclerotic disease were sometimes associated with thyrotoxic heart disease in the older age groups. In some cases the appearance of these complications was responsible for the production of symptoms referable to the heart. Generally the thyroid symptoms preceded the cardiac symptoms, but in some cases both appeared simultaneously. In 18 cases out of the 150 in this series the thyrotoxicosis was masked and only cardiac symptoms were obvious.

The basis of treatment is treatment of the thyrotoxic state. Thyrotoxic heart disease is considered one of the few cardiopathies totally reversible by treatment.

The authors prefer thyroidectomy to thiouracil treatment in advanced cardiopathy, and in early cases if there is a complicating organic factor such as hypertension or a disturbance of rhythm. Digitalis action is irregular in thyrotoxic heart disease. It is difficult to lower the pulse rate, and with heavy dosage the electrocardiogram often shows evidence of toxicity rather than bradycardia, a fact useful in the diagnosis of masked thyrotoxicosis. Quinidine is only useful after thiouracil treatment or operation, if the arrhythmia persists. *J. J. Giraldi*

652. **Acute Cor Pulmonale in the Absence of Pulmonary Embolism**

I. MACK, R. HARRIS, and L. N. KATZ. *American Heart Journal* [*Amer. Heart J.*] **39**, 664–677, May, 1950. 4 figs., 43 refs.

Acute cor pulmonale is due to a sudden increase in right ventricular work. The electrocardiographic changes are due to increased burden on the right ventricle and also to myocardial ischaemia of the right ventricle and posterior wall of the left ventricle. The sudden right-heart dilatation causes clockwise rotation round the long axis. Myocardial ischaemia results from a variety of causes: (1) Reduced coronary flow due to: (*a*) Increase in right ventricular and right auricular pressure, resulting in impaired drainage of the coronary sinus and the Thebesian veins. The increased intramural pressure in the right ventricle is also important. (*b*) Fall in left ventricular output, and hence in coronary artery flow, because flow through the lungs is diminished. The pressure gradient from coronary ostium to right auricle and right ventricle is diminished. (*c*) Tachycardia ultimately diminishing cardiac output and coronary flow by reducing diastolic filling time. (*d*) Reflexes such as the pulmono-pulmonary reflex, diminishing blood flow through the lungs by causing vasoconstriction. Increased pulmonary artery pressure also results from hypoxaemia. Peripheral circulatory failure causes pulmonary oedema and this reduces the flow through the lungs. (2) Incomplete oxygenation of blood in the lungs, because: (*a*) rapid, shallow breathing occurs; (*b*) the original lung condition usually impairs respiratory exchange. (3) Requirement by the heart of increased oxygen to do increased work, resulting from pulmonary hypertension and from the commonly co-existent fever. These combined factors may lead to death from heart failure.

The authors discuss the electrocardiographic changes in some detail and ascribe these to a combination of cardiac clockwise rotation round the long axis and myocardial ischaemia causing intraventricular block or right bundle-branch block. They stress the frequency of arrhythmias. They report 2 cases of pulmonary tuberculosis in which acute cor pulmonale developed after lung resection or thoracoplasty, and 1 case of acute cor pulmonale complicating bronchial neoplasm. In all 3 there was no pulmonary embolism. They stress the importance of recognizing non-embolic acute cor pulmonale, and mention sudden development of left-to-right shunts in the circulation, as exemplified by rupture of an infarcted interventricular septum and rupture of an aortic aneurysm into the right ventricle.

John Anderson

653. **The Syndrome of Cardiopulmonary Schistosomiasis (Cor Pulmonale)**

M. R. KENAWY. *American Heart Journal* [*Amer. Heart J.*] **39**, 678–696, May, 1950. 11 figs., 15 refs.

Seven cases of bilharzial cor pulmonale are described. In one of the patients necropsy was performed and the detailed pathological findings recorded. In the myocardium of this patient scattered foci of cellular infiltrations consisting mainly of lymphocytes, some histiocytes, fibroblasts, and eosinophile cells were demonstrated. No bilharzia ova were seen. The clinical, radiological, and electrocardiographic findings are fully described. Stress was laid on the possible diagnosis of concomitant pulmonary bilharzial infiltrations and their radiological appearances. Diagnosis of early cases can be made and confirmed radiologically. The *x*-ray appearance is that of the well-known " mitral configuration ".

The responsible lesions are mainly vascular, consisting of obliterative arteriolitis, produced by the passage of bilharzia ova through the arteriolar wall in an attempt to form extravascular parenchymatous tubercles. Healing of the intimal and medial lesions results in obstruction, which in some arterioles is complete. This is eventually followed by dilatation and atheroma of the main pulmonary artery and by marked hypertrophy of the right ventricle. In advanced cases the occluded tissue becomes canalized and expanded by capillary or cavernous formations to form the " angiomatoid " which is a characteristic feature of bilharzial arteriolitis.

The symptomatology is discussed. Haemoptysis was observed in 2 patients in the series. It is stressed that the term " Ayerza's disease " is unfortunately applied. A better terminology is " cardiopulmonary bilharziasis " or, still better, " bilharzic cor pulmonale ".

Cyanosis is not a constant feature of the syndrome and is only present when heart failure sets in, or if there is concomitant pulmonary infection with septic organisms (such as chronic bronchitis). Clubbing of the digits is also not constant, but may be present in a good number of patients.—[From the author's summary.]

[This is a useful paper giving information on a hitherto obscure subject.—EDITOR.]

654. **The Origin of Oedema in Heart Failure**

J. BROD and Z. FEJFAR. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **19**, 187–220, July, 1950. 18 figs., 28 refs.

The cardiac output, right auricular pressure, renal blood flow, glomerular filtration rate, urine volume, volume of packed cells, serum protein concentration, and blood volume (by the Evans-blue method) were estimated over periods of up to 12 hours in 10 control subjects and 25 patients with heart disease. The purpose of the study was to determine whether spontaneous fluctuations in urine flow could best be explained on the basis of the forward-failure or backward-failure theory. The evidence suggested that the former was correct, for spontaneous changes in urine flow were not preceded by any consistent change in right auricular pressure or cardiac output. A fall in right auricular pressure and transient haemoconcentration followed diuresis in subjects with

cardiac failure. In the patients with cardiac failure, but not in the control group, the rate of urine flow regularly changed in the same direction as the renal blood flow and glomerular filtration rate. In patients with moderate degrees of cardiac failure the renal blood flow and urine flow are reduced during the day, presumably to divert blood to more vital organs (" emergency distribution of available blood "), but increase at night when the patient is at complete rest. In very severe grades of failure the " emergency distribution " persists day and night.

G. M. Bull

655. **The Excretion of Chlorides in Patients with Heart Failure**

Z. FEJFAR and J. BROD. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **19**, 221–237, July, 1940. 2 figs., 17 refs.

In addition to the observations reported in the previous paper (Abstract 654), chloride concentrations in plasma and urine were determined. The spontaneous nocturnal diuresis of patients with cardiac failure was accompanied by an increased concentration of chloride in the urine. The resulting increase in chloride output was out of proportion to the simultaneous increase in glomerular filtration and filtered load of chloride delivered to the tubules. This suggested that the tubular chloride reabsorption diminished during the diuresis. The extent of this reabsorption varied considerably from patient to patient and was greater in patients in cardiac failure than in control subjects. In one control subject and one patient with cardiac failure an increase in water excretion was not accompanied by an increase in chloride excretion. In both these cases this may have been due to the fact that the patient drank water about half an hour before.

The results are interpreted as showing that the low output of chloride in cardiac failure is the result of a diminished chloride load. It is suggested that the increase in chloride excretion which accompanies diuresis in these patients occurs because of the more rapid urine flow through the distal convoluted tubule with shorter contact of the ion with the reabsorbing tubular cells. [The findings can be interpreted in other ways. The last suggestion is unlikely if water diuresis was not associated with increased chloride loss in all subjects. However, this and the preceding paper add important factual data to our knowledge of oedema in heart failure.]

G. M. Bull

656. **Can Systolic Expansile Pulsation of the Auricle be Taken as a Criterion of Mitral Incompetence?** (L'expansion systolique auriculaire peut-elle être prise comme critère d'insuffisance mitrale?)

R. FROMENT, A. GONIN, and L. GALLAVARDIN. *Archives des Maladies du Cœur et des Vaisseaux* [*Arch. Mal. Cœur*] **43**, 678–686, Aug., 1950. 9 refs.

The radiological finding of systolic expansion of the left atrium in a patient with suspected mitral disease is usually taken as proof of mitral incompetence. The correctness of this opinion is questioned by the authors. They point out that of the cases of mitral disease reported by Lenègre there were 19 which did not show systolic expansion of the left auricle; of these, 4 patients had characteristic murmurs of mitral incompetence. There were 52 with systolic expansion of the left auricle, but of these 10 had no systolic murmur and were thought on clinical grounds to have pure mitral stenosis. The authors' doubts appeared to be confirmed by a case of systolic expansion of the left antrium which they record. At necropsy the valves, though stenosed, were completely competent.

The conclusion of the authors is that systolic expansion of the auricle is not pathognomonic of mitral regurgitation, but is mostly due to an upward movement of the atrio-ventricular septum during ventricular systole. The sign is not one of mitral incompetence but of mitral disease and consequent dilatation of the left atrium.

H. E. Holling

657. **Arrhythmias during Intracardiac Catheterization**

J. MICHEL, A. D. JOHNSON, W. C. BRIDGES, J. H. LEHMANN, F. GRAY, L. FIELD, and D. M. GREEN. *Circulation* [*Circulation*] **2**, 240–244, Aug., 1950. 5 figs., 5 refs.

Intracardiac catheterization in 133 patients caused arrhythmia in 37% of the cases. The site of origin of the arrhythmia frequently differed from the site of the catheter tip and, in a number of cases, disturbances such as auricular fibrillation were provoked by a catheter that had not penetrated beyond the axillary vein. The only fatality in this series occurred as a combined effect of thiopentone administration and an attempt at catheterization in which the catheter never reached the heart.

G. Schoenewald

658. **Ventricular Tachycardia during Cardiac Catheterization of Patient with Wolff–Parkinson–White Syndrome. Report of a Case showing Effects of Atropine Sulfate**

R. A. BRUCE, P. N. G. YU, F. W. LOVEJOY, M. E. MCDOWELL, and R. PEARSON. *Circulation* [*Circulation*] **2**, 245–249, Aug., 1950. 2 figs., 17 refs.

Cardiac catheterization in a patient with the Wolff–Parkinson–White syndrome and a probable mitral lesion caused a most alarming attack of multifocal paroxysmal ventricular tachycardia lasting for many hours. After all other measures had failed, intravenous injection of 1·2 mg. of atropine sulphate promptly changed ventricular to supraventricular tachycardia, and later to a sinus rhythm.

G. Schoenewald

659. **A Study of the V Leads in Congenital Heart Diseases, with Particular Reference to Ventricular Hypertrophy and its Diagnostic Value**

M. SOKOLOW and A. L. EDGAR. *American Heart Journal* [*Amer. Heart J.*] **40**, 232–251, Aug., 1950. 12 figs., 5 refs.

Unipolar extremity and precordial electrocardiograms were recorded in 153 cases of proven congenital heart disease. Among the 39 cases of patent ductus arteriosus included, the electrocardiogram was normal in 21 and showed evidence of left ventricular hypertrophy in 17 and of right bundle-branch block in one. Of 12 cases in which the ductus was larger than 1 cm. in diameter left ventricular hypertrophy was recorded in 9, suggesting that in patent ductus arteriosus left ventricular hyper-

trophy is a function of the width of the ductus and hence provides an indication of the size of the shunt. Among the 32 cases of coarctation of the aorta the electrocardiogram was normal in 6 and showed evidence of left ventricular hypertrophy in 19, of right bundle-branch block with left ventricular hypertrophy in 2, and of right ventricular hypertrophy in 5 cases (in all of which some additional defect was present). Of the 8 cases of interauricular septal defect 5 had electrocardiographic signs of right ventricular hypertrophy and 3 of incomplete right bundle-branch block; none showed signs of left ventricular hypertrophy. Of the 40 patients with uncomplicated Fallot's tetralogy 39 showed signs of right ventricular hypertrophy. Of the other 31 patients in the cyanotic group 25 had right ventricular hypertrophy, while 6 had left ventricular hypertrophy. This last group consisted of 3 cases of tricuspid atresia with non-functioning right ventricle, 2 of Fallot's tetralogy and large patent ductus arteriosus, and one of truncus arteriosus and patent ductus arteriosus.

William A. R. Thomson

660. **Congenital Mitral Atresia, Transposition of the Great Vessels, and Congenital Aortic Coarctation. A Case Report and an Interpretation of the Anomaly**
H. L. BROCKMAN. *American Heart Journal* [*Amer. Heart J.*] **40**, 301–311, Aug., 1950. 4 figs., bibliography.

The heart of a negro child who died suddenly 36 hours after normal birth was found at necropsy to have no mitral orifice. The heart was enlarged; both atria were present, the right being dilated and the left small, and the veins drained normally into them. The mitral orifice was completely absent and not even a rudimentary left ventricle could be found. There was no evidence of foetal endocarditis. The common ventricle was considerably hypertrophied. Externally the aorta and pulmonary artery were incompletely separated at their origin, but each valvular orifice had three semilunar valves. The aorta was stenosed distal to the left subclavian artery. The pulmonary artery gave off left and right branches, but a trunk (the ductus arteriosus) continued as an arching vessel continuous with the descending aorta. The coronary arteries opened above the aortic valves, but their course was abnormal as a result of excessive rotation of the bulbus cordis during formation of the heart. The right coronary artery arose ventrally and the left dorsally, the posterior descending branch of the right coronary artery running down the ventral surface of the heart and the left coronary artery along the dorsal surface.

It is presumed that at about the 6th week of development fixation of the bulbus to the atrial canal failed to occur. This permitted the canal to shift to the right so that the septum primum came to lie over the mitral orifice. Fusion occurred, therefore, between the septum primum, the fused dorsal and ventral endocardial cushions, and the lateral endocardial cushion. The same excessive clockwise torsion permitted the moving of the dorsal wall of the bulbus to the right, and so placed the aorta in its right ventral position.

The literature of the condition (48 reported cases) is reviewed. *H. E. Holling*

661. **Rupture of Pulmonary Aneurysm Accompanying Patent Ductus Arteriosus. Occurrence in a 67 Year Old Woman**
M. C. F. LINDERT and H. L. CORRELL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 888–891, July 8, 1950. 2 figs., 31 refs.

ENDOCARDITIS

662. **Serous Endocarditis in Children.** (Seröse Endokarditis bei Kleinkindern und Jugendlichen)
R. BÖHMIG. *Virchows Archiv für Pathologische Anatomie und Physiologie* [*Virchows Arch.*] **318**, 646–687, 1950. 15 figs., bibliography.

The author, who is Director of the Municipal Pathological Institute at Karlsruhe, has traced the origin of non-rheumatic valve lesions of the heart back to childhood in previous papers, and in the present paper, based on the morbid anatomical and histological study of 108 hearts from subjects ranging in age from 0 to 18 years, he describes a condition which he considers to be the fundamental basis of all such lesions, and which he calls " serous endocarditis ". This is, he believes, a form of Rössle's " serous inflammation ". The characteristic lesions are found in the endocardium as minute foci of cellular damage or of endothelial proliferation, in the subendothelial tissues as diffuse or warty myxomatoid swellings with or without sparse inflammatory cells, and in the central layers of the valve as oedematous swelling with loss (or increase) of elastic and collagen fibres. He suggests that all valvular lesions at later ages, including probably the rheumatic, can be traced to recurrence of this inflammation. Bacterial infection, toxins of other origins, or metabolic disorders may be aetiological factors: details are given of a number of cases in which diverse diseases were associated with a post-mortem finding of serous endocarditis. Indeed, the author states that it is very unusual, even in the youngest age groups, to find a heart without such lesions.

[Acceptance of the basic thesis of this paper depends on one's attitude to Rössle's serous inflammation, a concept which has been applied very widely by German pathologists, but which elsewhere has found little favour —though it must be admitted that it seems to have been little studied.] *Bernard Lennox*

663. **Therapeutic Experiences with Subacute Bacterial Endocarditis, with Special Reference to the Failures**
D. LITTMANN and R. S. SCHAAF. *New England Journal of Medicine* [*New Engl. J. Med.*] **243**, 248–252, Aug. 17, 1950. 9 refs.

Cases of subacute bacterial endocarditis treated at the Massachusetts General and West Roxbury Veterans Administration Hospitals are discussed. Comparison of the cases treated in 1944–46 with those treated in 1947–49 shows that the disease incidence has fallen by almost half, but the condition has become more resistant to treatment by antibiotics. This change is thought to be due to the increasing use of antibiotics for other comparatively trivial ailments, resulting in the cure of

undiagnosed cases of endocarditis and increased resistance to antibiotics in the remaining cases.

Not a single instance of bacterial endocarditis superimposed on coarctation of the aorta occurred in this series of 97 cases. A congenital bicuspid aortic valve was a frequent underlying lesion in fatal cases.

Death was more frequently due to irreversible cardiac, renal, or cerebral changes than to failure to combat the infection. This indicates that the infection should be recognized early and adequately treated if the outcome is to be successful. *H. E. Holling*

664. **Streptomycin in Subacute Bacterial Endocarditis. Report of Three Cases**
P. H. WILLCOX. *Lancet* [*Lancet*] **2**, 288–290, Aug. 19, 1950. 3 figs., 3 refs.

In cases of subacute bacterial endocarditis where adequate penicillin therapy proves unsuccessful, streptomycin is worthy of trial. Three cases of subacute bacterial endocarditis are reported [diagnosed on clinical grounds alone, with repeatedly negative blood cultures] in which doses of penicillin up to 12 mega units daily failed to produce remission of fever or improvement, yet streptomycin (2 to 6 g. daily) effectively controlled the infection. It is urged that resort should be made in such cases to streptomycin when the infecting organism is penicillin-insensitive or when skin reactions to penicillin prove troublesome. *J. L. Lovibond*

665. **After-history of Successfully Treated Cases of Subacute Bacterial Endocarditis**
H. MATTHEW. *British Medical Journal* [*Brit. med. J.*] **2**, 436–439, Aug. 19, 1950. 22 refs.

Twenty cases of subacute bacterial endocarditis have been closely followed up for 27 to 63 months after treatment with penicillin. No case relapsed or became reinfected. One patient died. Of the remainder, one developed a hemiplegia, and one congestive heart failure, but the rest are working as hard as before their illness. Four have married and 2 have borne children without difficulty.

No heart whose size before treatment was normal became enlarged. In 4 cases the heart increased in size during treatment, but no regression or further enlargement has been noted. One patient has acquired aortic incompetence since infection. No others show auscultatory evidence of fresh valvular damage. Three patients developed paroxysmal auricular fibrillation, one frequent ventricular extrasystoles. In 2 cases of infection of congenitally stenosed pulmonary valves exercise tolerance has now increased. The difficulty of assessing the relative roles of bacterial and rheumatic infection is stressed. *D. Verel*

666. **Rheumatic Heart Disease in Service Pensioners. A Review of 318 Cases**
R. HARTLEY. *British Medical Journal* [*Brit. med. J.*] **2**, 396–398, Aug. 12, 1950. 6 refs.

A follow-up study was made of 318 men discharged from the Services with rheumatic heart disease. All presumably had the disease on entry. In only 5 was an apical systolic murmur noted on enlistment, indicating the correctness of assessment of the many men with incidental systolic murmurs accepted for service. The author is of the opinion that most of his 318 cases could have been diagnosed on entry, failure to make an adequate clinical cardiological examination being responsible for their acceptance. The incidence of aortic valve lesions in the series was very high (74%), due probably to the greater difficulty in the diagnosis of these lesions than in the diagnosis of mitral lesions. A history of previous rheumatic infection was obtained in only 37% of the cases.

Recurrence of rheumatic fever led to the diagnosis in 31% of the cases. The " expected " recurrence rate for this age group is 5%. Possibly the rigours of training increased the predisposition to recurrences, half of which occurred within 2 years of entry. Dyspnoea on effort was the presenting symptom in 27% of the cases, but in none did it appear to be precipitated by Service training. A third of the cases were symptom-free, being discovered on routine examination, although no less than 80% of the patients developed symptoms within 6 months of diagnosis owing to a superimposed cardiac neurosis. Only 5% reported with haemoptysis; in many of these cases unnecessary lung investigations were carried out. Five entered sanatoria. Mass radiography accounted for the diagnosis in 5 cases, and bacterial endocarditis led to diagnosis in 4 and congestive failure in one.

Antero-posterior chest radiographs were taken of 264 of the patients after diagnosis. The heart was reported as enlarged in 81% and normal in the remainder. The high percentage of cases in which the heart was said not to be enlarged would probably have been reduced had oblique views been taken. *Ellis Dresner*

CORONARY INSUFFICIENCY AND ANGINA

667. **Effect of Blood Cholesterol Disorders on the Coronary Arteries and Aorta**
L. M. MORRISON and W. F. GONZALEZ. *Geriatrics* [*Geriatrics*] **5**, 188–195, July–August, 1950. 7 figs., bibliography.

The post-mortem findings in a series of 590 patients, aged 20 to 75 years, who had died of various diseases at the Los Angeles County General Hospital were examined and analysed. Any atheromatous change reported in the coronary arteries and aorta was graded into four degrees of severity according to the pathologist's description.

The cases were selected from the post-mortem records in chronological order in six groups, one consisting of cases of diabetes mellitus, which is associated with hypercholesterolaemia, and another of cases of chronic thyrotoxicosis, which is associated with hypocholesterolaemia. The four other groups, which were used as controls, consisted of cases of acute illness and sudden death, of chronic illness, of cancer, and of alcoholic cirrhosis of the liver. The findings are analysed statistically, both as to validity of sampling and significance.

Patients dying from diabetes mellitus showed more advanced atheroma, occurring at a younger age, than

the control groups, whereas the patients dying of chronic thyrotoxicosis had a less severe degree of atheroma than the controls. It is suggested that the results indicate that disturbances of cholesterol metabolism may be a factor in the aetiology of coronary and aortic atheroma in man.

P. D. Bedford

668. **The Interrelationships of Serum Cholesterol, Cholesterol Esters and Phospholipids in Health and in Coronary Artery Disease**

M. M. GERTLER, S. M. GARN, and J. LERMAN. *Circulation* [*Circulation*] **2**, 205–214, Aug., 1950. 1 fig., bibliography.

In this work three groups of subjects were studied: 97 males under the age of 40 years with coronary artery disease, 146 healthy males of comparable ages, and a matched group of 97 men each of whom corresponded closely in height, weight, age, body build, ethnic origin, and occupation to one of the first group; the mean total serum cholesterol values were 286, 224, and 247 mg. per 100 ml. in these groups respectively. The maximum difference was found in the values for serum cholesterol esters, the higher total value in coronary disease therefore reflecting the altered ester level. The serum phospholipid level was also higher in patients with coronary disease.

W. S. Killpack

669. **Blood Lipids and Human Atherosclerosis**

J. W. GOFMAN, H. B. JONES, F. T. LINDGREN, T. P. LYON, H. A. ELLIOTT, and B. STRISOWER. *Circulation* [*Circulation*] **2**, 161–178, Aug., 1950. 22 figs., 15 refs.

By means of the ultracentrifuge four classes of large cholesterol-bearing lipid and lipoprotein molecules were identified in human serum, and high values for one class of molecule were found to be frequent in certain diseases and in the rabbit fed on cholesterol.

These molecules do not participate in the ordinary post-prandial lipaemia, and their concentration is not related in any way to the serum cholesterol content as estimated by the usual biochemical methods; it is, however, affected by long-term dietary restriction. The first group of patients selected for study had all survived an unequivocal myocardial infarction for 6 weeks or more; the large cholesterol molecules were present in higher concentration and with greater frequency than in persons of similar ages without evidence of atheromatous vascular disease. An increased frequency was also found in diabetes mellitus, the nephrotic syndrome, and hypothyroidism.

W. S. Killpack

670. **Pain Patterns in Acute Myocardial Infarction**

J. H. BEHRMANN, H. R. HIPP, and H. E. HEYER. *American Journal of Medicine* [*Amer. J. Med.*] **9**, 156–163, Aug., 1950. 3 figs., 11 refs.

In 150 well authenticated cases of myocardial infarction the relation of the duration, location, radiation, and mode of onset of pain to the mortality rate was studied.

It is pointed out that the taking of a full clinical history with reference to these points is of the utmost importance in establishing an early diagnosis of cardiac infarction, but that it is difficult to assess the ultimate prognosis from them. The investigators suggest that, if the cases of severe pain and death before the patient is seen by a doctor are disregarded, there does appear to be some relation between the duration of the pain and the gravity of the prognosis; pain of over 24 hours' duration is associated with the highest mortality (38·7%). In cases in which pain is limited to the thorax the prognosis is worse than when pain radiates to the neck and limbs. It is suggested that in the former cases the infarction is more dangerous, producing a greater degree of shock and therefore a lessened perception of pain.

The authors point out, however, that these relations are by no means constant.

J. B. Wilson

671. **Anticoagulants in Myocardial Infarction**

F. J. SCHILLING. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 785–789, July 1, 1950. 15 refs.

672. **The Abuse of Bed Rest in the Treatment of Myocardial Infarction**

C. W. IRVIN and A. M. BURGESS. *New England Journal of Medicine* [*New Engl. J. Med.*] **243**, 486–489, Sept. 28, 1950. 27 refs.

Despite the fact that there is no statistical evidence that rest in bed or even restriction of activity over a prolonged period is advantageous in the treatment of myocardial infarction, most authorities advise 4 or more weeks of complete rest in bed. The advantages ascribed to this are avoidance of anoxia due to shock, prevention of sudden death, and preservation of myocardial function. The first necessitates a brief recumbency. Sudden death may be due to rupture of the myocardium, but this usually occurs during the first 2 weeks and there is evidence that necrotic muscle has been completely replaced by connective tissue at the end of this period. There are, however, some hearts which show no evidence of healing after 3 to 5 weeks; these patients would probably not survive under any conditions. Another cause of sudden death is the abrupt appearance of arrhythmias, but these tend to occur even earlier in convalescence. The functional capacity of the heart after recovery depends mainly on the amount of effectively contractile heart muscle that remains, the area of scar tissue being of less importance. An aneurysm of the scar, causing waste of ventricular effort because of its elasticity, is probably disadvantageous, but no convincing evidence has been presented that early resumption of activity would favour aneurysm production.

The disadvantages of recumbency are that the circulation to the basal part of the lung is poor; atelectasis, hypostatic pneumonia, and constipation are common sequels. Congestive failure may become worse and some authorities consider the sitting position more favourable for patients with angina pectoris. Phlebothrombosis and subsequent embolism is much commoner. In normal young volunteers prolonged rest in bed markedly decreases exercise tolerance, produces abnormality of calcium and nitrogen metabolism, and affects the mechanism maintaining adequate circulation on standing, as indicated by an increased tendency to faint in tilt-table tests. The psychological effect of confinement to bed

is bad, and many patients are rendered inactive by symptoms brought on by fear rather than by heart disease.

For the majority of patients the authors recommend 2 weeks in bed with reasonable, carefully explained restrictions and possibly bedside toilet privileges, followed by progressive walking exercise for 2 weeks.

R. Hodgkinson

673. **Lipid Interrelationship in Health and in Coronary Artery Disease**

M. M. GERTLER and S. M. GARN. *Science* [*Science*] **112**, 14–16, July 7, 1950. 10 refs.

674. **A Method for the Evaluation of the Effects of Drugs on Cardiac Pain in Patients with Angina of Effort. A Study of Khellin (Visammin)**

T. GREINER, H. GOLD, M. CATTELL, J. TRAVELL, H. BAKST, S. H. RINZLER, Z. H. BENJAMIN, L. J. WARSHAW, A. L. BOBB, N. T. KWIT, W. MODELL, H. H. ROTHENDLER, C. R. MESSELOFF, and M. L. KRAMER. *American Journal of Medicine* [*Amer. J. Med.*] **9**, 143–155, Aug., 1950. 15 refs.

The value of dimethoxy-methyl-furano chromone (khellin) in the treatment of angina of effort was investigated. This investigation, which was carefully controlled, demonstrated that khellin has no beneficial effect on angina of effort. In the dosage used (approximately 50, 100, or 150 mg. daily) side-effects were few and of relatively little importance.

The main part of the article deals with the methods by which the investigations were controlled. The fallacies inherent in previous investigations into the treatment of angina of effort are discussed, and it is shown how most of these fallacies were overcome in the cases investigated.

The dosage of khellin was controlled with dextrose tablets; neither the patient nor the doctor assessing the treatment knew which the patient was having. Use was made of " daily report cards " and the authors consider that study of these gave much more accurate results than could be obtained by " interval evaluation ", that is, assessment of progress by discussion at the end of a certain period. Some evidence is advanced to prove the inadequacy of this latter method.

Over periods of 3 months 39 patients were treated, the use of the " daily report card " providing accurate information easily assessable for statistical purposes. It is suggested that a similar method could be used to evaluate the effect of drugs on a symptom involving other organs.

J. B. Wilson

675. **The Treatment of Angina Pectoris with a Preparation of Khellin (Ammi Visnaga)**

C. A. ARMBRUST and S. A. LEVINE. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220**, 127–132, Aug., 1950. 10 refs.

Khellin was given in 40-mg. tablets by mouth three times a day to 53 patients suffering from angina of effort, alternating in 28 of them with administration of a placebo, neither patient nor doctor knowing which was the active preparation. About 60% of cases showed improvement; there were fewer and milder anginal attacks, less nitroglycerin was used, and the patient could walk farther. Nausea, anorexia, and dizziness occurred in 60% of cases. The authors discuss the difficulty of assessing the value of therapy in angina, but conclude that khellin is useful in this condition.

D. Verel

676. **Multiple Lead Electrocardiograms in Angina Pectoris**

J. E. F. RISEMAN and B. N. JOSEPHS. *American Heart Journal* [*Amer. Heart J.*] **40**, 260–270, Aug., 1950. 17 refs.

Three bipolar standard leads (I, II, III), three augmented unipolar limb leads (aVL, aVR, aVF), and six unipolar precordial leads (V_1 to V_6) were recorded in 100 patients with angina pectoris but no previous history of myocardial infarction, 34 patients with angina pectoris and a previous history of myocardial infarction, and 100 individuals over the age of 45 years with no symptoms or signs of heart disease. Normal electrocardiograms were recorded from 85 of the 100 control subjects, 52 of the 100 patients with no previous history of infarction, and 7 (21%) of those with such a history. No constant relationship was noted between the electrocardiographic findings and the size of the heart or the blood pressure. The abnormalities recorded in the normal group and among those with angina pectoris were comparable, and it was impossible to say from the electrocardiogram alone whether or not the patient was subject to angina pectoris. The most frequent abnormalities found were inverted, diphasic, or absent T waves in leads I, V_5, and V_6. Abnormal Q waves were most common in patients with a previous history of myocardial infarction.

William A. R. Thomson

DISORDERS OF CIRCULATION

677. **Tropical Thromboangiitis of the Splenic Vessels and its Relationship to Primary Splenic Abscess**

M. GELFAND. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. R. Soc. trop. Med. Hyg.*] **44**, 117–121, July, 1950. 2 figs., 10 refs.

The author has followed up the original work of Fisher *et al.* (*J. Path. Bact.*, 1947, **59**, 405) on tropical thrombophlebitis. These authors reported 2 cases of splenic-vein involvement, and splenic abscess has been recognized as a clinical entity in South Africa since a report by Wallace in 1922. The case recorded is that of an adult African male, admitted in semi-delirium with a temperature of 100·4° F. (38° C.). He died 48 hours later. Blood smears had been negative for malaria and relapsing fever, and the Wassermann reaction was negative. The protein content of the cerebrospinal fluid was increased to 80 mg. per 100 ml. Necropsy revealed a mass 10×8 in. (25·4×20·3 cm.) under the left diaphragm, filled with 3 pints (1·7 litre) of blood. The capsule consisted of necrotic splenic pulp. The whole length of both splenic vein and artery was thrombosed, the thrombosis in the vein being the older. Eosinophilic bodies were not detected in the intima. The pathological process would

appear to have been thrombophlebitis and arteritis with colliquative necrosis of the spleen, which would probably have become infected if death had not supervened. It is suggested that thrombophlebitis is a much more probable cause of splenic abscess in subtropical Africa than amoebiasis, which has hitherto been regarded as the usual cause. *Clement Chesterman*

678. **The Ophthalmoscopical Appearance of the Fundus Oculi in Elderly Persons with Arterio-sclerosis and Normal Blood Pressures**
H. VOGELIUS and P. BECHGAARD. *British Journal of Ophthalmology* [*Brit. J. Ophthal.*] **34**, 404–408, July, 1950. 7 refs.

A series of 124 persons all over 40 and with normal blood pressure were examined ophthalmoscopically.

Changes due to arteriosclerosis (abnormal arteriovenous crossings and slight irregularities of calibre) were found even in the 40- to 50-year age group, but narrowing of the arteries and marked irregularity were found with greater frequency with increasing age. Only in one patient below 60 years were the changes marked. In no case was haemorrhage, exudate, or papilloedema seen. In all cases the veins were normal. Thus, constriction and irregularity of arteries in the elderly occur frequently quite apart from hypertension. *D. Ainslie*

HYPERTENSION

679. **The Morbid Anatomy of the Brain in Hypertension.** (Патологоанатомические изменения в головном мозгу при гипертонической болезни)
A. S. OGURTSOVA. Невропатология и Психиатрия [*Nevropat. Psikhiat.*] **19**, No. 3, 67–74, May–June, 1950. 6 figs.

The author studied the cerebral arteries and the brain in 37 cases of hypertension. She concludes that the spread of the lesions and their intensity were related to the duration of the hypertension. The arterial changes tended to be more marked along the course of the branches of the middle cerebral artery. Diapedesis of erythrocytes was common. Nerve cells were most degenerate in the 2nd and 3rd layers of the frontal lobes, the inferior olives, the reticular formation, and the dentate nucleus. The character of the lesions was suggestive of the effect of toxaemia in addition to anoxia. *L. Crome*

680. **Ophthalmological Investigations of 500 Persons with Hypertension of Long Duration**
P. BECHGAARD, K. PORSAA, and H. VOGELIUS. *British Journal of Ophthalmology* [*Brit. J. Ophthal.*] **34**, 409–424, July, 1950. 8 figs., 7 refs.

In this survey only cases of long-standing hypertension were investigated and therefore cases of malignant hypertension were automatically excluded.

A series of 485 patients with persistently raised blood pressure of at least 160/100 mm. Hg for from 4 to 11 years were examined. The ophthalmoscopic examinations were all made by an ophthalmologist after mydriasis. In 160 cases the retinal vessels were normal. In only one case was there oedema of the disk, and in 30 cases haemorrhages and exudates were found. Thus the severe degrees of retinopathy were rarely seen. In 50% of patients the arterial diameters were normal, but the vessels were narrow in 34%. In 27% of cases there was marked irregularity, and in 7% of cases indentation of the veins by the arteries was seen at the points of crossing.

The course of the arteries was normal in 72% of cases: the most usual abnormality was the presence of gentle curves. Minor alterations in the arterial reflex were found in 46% of cases but copper-wire arteries and sheathing in only 4%. No silver-wire arteries were seen.

It is noted that the condition of the fundus is not necessarily connected with the general condition of the patient. Normal fundi were found in cases severely affected by hypertension, and general symptoms and signs were often slight in cases showing advanced retinal change. *D. Ainslie*

681. **The Normal Blood Pressure Range and its Clinical Implications**
A. M. MASTER, L. I. DUBLIN, and H. H. MARKS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 1464–1470, Aug. 26, 1950. 2 figs., 36 refs.

An attempt was made to assess the normal range of blood pressure. Figures based on records of 15,706 people (males and females roughly equal), ranging in age from 12 to 65 and working in 16 different industries, are analysed. The data may be summarized as follows.

Between the ages of 25 and 29 the average systolic blood pressure was 8 mm. Hg higher in men than in women, and the diastolic pressure 4 mm. higher. Thereafter the difference gradually diminished and after 45 was negligible. In men the normal range of systolic pressure at age 16 was 105 to 135 mm. with a diastolic range of 60 to 86 mm. At ages 60 to 64 the systolic range was 115 to 170 mm. with a diastolic range of 70 to 100 mm. Women at 16 years had a systolic range of 100 to 130 mm. and at 60 to 64 years of 115 to 175 mm., with a diastolic range of 65 to 85 mm. at 16 years and 70 to 100 mm. at 64 years. The authors consider that the lower limit for systolic pressure in hypertension is 145 mm. at 16 to 18 years, 150 mm. at 19 years, and 155 mm. at 30 to 34 years. It then increases by about 5 mm. every 5 years and at 60 to 64 years 190 mm. is the lower limit. In women the lower limit is 140 mm. up to the age of 30, thereafter increasing by 5 to 10 mm. every 5 years, and at 45 years is higher than in men, but at 60 to 64 years it is the same in both sexes. A systolic pressure below 99 mm. is probably abnormal in men aged 16 to 24, and a reading below 108 mm. is probably abnormal in the age group 60 to 64. In women the pattern is much the same.

There was no relation between height and blood pressure, but weight was an important and consistent factor regardless of age or sex. The effect of obesity was most marked in women over 40. The authors attempt to assess the frequency of hypertension. Obviously, figures will vary considerably according to the definition of hypertension adopted. The authors analyse their figures by several different criteria. By any

standard the figures show that incidence of hypertension increases steadily with age. If a blood pressure of 140/90 mm. Hg be taken as the upper limit of normal after the age of 20 (as is often done), 20% of men between 20 and 29 years are hypertensive (although only about 5% had readings above 150/100) and 40% of men and women between 45 and 49 years and 60% between 60 and 64 years. If 150/100 mm. Hg be taken as the upper limit of normal, nearly 20% of people by the age of 45 are hypertensive, and over 35% between the ages 60 to 64. These figures conform closely with previously published detailed statistics compiled by the authors. How can what is seen so frequently in people without symptoms be regarded as abnormal? An almost universal blood-pressure phobia has been created because of the huge number of people said to be hypertensive. Many over the age of 50 with systolic pressures of 160 to 190 and diastolic of 100 to 110 mm. have been unwarrantably alarmed by their physicians and have been subjected to dietary, medicinal (often dangerous), and even surgical procedures.

[This is a very good paper and should be read by all, especially surgeons, who are interested in the treatment of hypertension. The statistical unit of the Medical Research Council might perhaps make an exhaustive survey of hospital records to determine the prognosis in relation to blood pressure readings. There are many unanswered questions about blood pressure which could possibly be solved by statistical survey of the records of hospital in-patients and out-patients.]

M. H. Pappworth

682. **Follow-up Study of One Hundred Private Hypertensive Patients with Cardiovascular Complications**

P. D. WHITE, E. G. DIMOND, and A. WILLIAMS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 1311–1317, Aug. 12, 1950. 4 refs.

The authors have compared the clinical course in 50 cases of hypertension complicated by heart failure, cerebrovascular accident, coronary thrombosis, or angina of effort in which sympathectomy was performed during the period 1941–46, with that in a control group of 50 similar cases not treated by operation. In all cases a lumbodorsal sympathectomy was performed by Smithwick, and the follow-up was carried out by White. Of the operated group the result was " excellent " (living, normotensive, no symptoms) in 6 cases, " good " in 5, and " fair " in 11; the condition was unchanged in 5 and worse in 11, and 12 patients have died, one from an unrelated cause. In the control group, 5 patients fall into the " excellent ", " good ", and " fair " categories, the condition of 4 is unchanged or worse, and 41 have died. but it is emphasized that the two groups are by no means comparable, only 7 of the patients in the control group having been considered suitable for sympathectomy. Of these 7, however, after 3 years 3 had died, 2 were bedridden, and 2 were unimproved. [It is not stated why the remaining control cases were unsuitable for sympathectomy.]

The cases in which sympathectomy was performed were reassessed according to revised criteria now in use and it was found that on this basis 13 patients would have been advised against operation. Of these in fact only one shows some improvement, while the remainder are worse or have died. Of the patients still considered to have been suitable for operation or borderline cases, 26 show an improvement, and 11 are worse or dead.

D. Verel

683. **Hypertensive Cardiovascular Disease (" Malignant Hypertension "). Changes in Canine Tissues Induced by Various Manipulations of the Kidney, with Special Reference to Vascular and Myocardial Lesions**

E. E. MUIRHEAD, A. GROLLMAN, and J. VANATTA. *Archives of Pathology* [*Arch. Path.*] **50**, 137–150, Aug., 1950. 5 figs., 21 refs.

The authors have previously shown that bilateral nephrectomy in the dog induces tissue changes comparable to those of malignant hypertension, as well as elevation of blood pressure. In this paper they show that the arterial and arteriolar necroses are independent of hypertension, circulatory failure, or uraemia, and may even occur when non-functional but morphologically normal kidneys are present.

The vascular changes were observed in dogs kept alive by dietary measures, use of the artificial kidney, exchange transfusion, or peritoneal dialysis after bilateral nephrectomy. They occurred also after ligation or section of the ureters, implantation of the ureters into the bowel or vena cava, or intraperitoneal injection of concentrated dialysed urine.

[This paper is itself a condensed record of a large number of experiments, and should be read in the original by those interested.] *Martin Hynes*

684. **Experimental Renal Hypertension and its Course following the Production of a Peripheral Arteriovenous Fistula**

R. A. DETERLING and H. E. ESSEX. *Annals of Surgery* [*Ann. Surg.*] **132**, 129–142, July, 1950. 4 figs., 28 refs.

Hypertension was produced in 27 dogs by wrapping each kidney in a square of silk cloth or cellophane in a 2-stage operation; after about 4 weeks the arterial pressure was markedly increased, the average being 270 mm. Hg systolic and 160 mm. diastolic, and the maximum 305 mm. systolic and 220 mm. Hg diastolic. Of a control group of 8 of these hypertensive dogs, 2 died in the malignant phase; widespread and marked pathological changes were noted in all 8 at necropsy. In the remaining 19 hypertensive dogs an extensive femoral arterio-venous fistula was established at operation 6 to 16 weeks after the renal operation; this was followed initially by a moderate fall in both systolic and diastolic pressure, but after the 10th day the readings rapidly returned to their previous high level, and in about half the dogs the systolic pressure, and in a quarter the diastolic pressure, had risen to even higher levels by the time of death. The cardiovascular and other changes resulting from the two lesions together were much more severe than from either lesion alone, and the mortality was likewise greater.

Joseph Parness

Disorders of the Blood

685. **Herpes Zoster and Leukaemia.** (Herpes zoster och leukämi)
B. E. HALLGREN. *Nordisk Medicin* [*Nord. Med.*] **44**, 1475–1478, Sept. 15, 1950. 18 refs.

During the last 3 years the author has seen, in the Uppsala University Hospital, 5 cases of herpes zoster associated with leukaemia (3 with myeloid and 2 with lymphatic leukaemia). In a sixth, myeloid leukaemia was not diagnosed until several years after an attack of herpes zoster, but may possibly have been present when the latter occurred. A further 60 cases have been collected from the literature, in 48 of which the coexisting leukaemia was of lymphatic type. In a discussion of the pathogenesis, the author considers the possibility that a virus causing leukaemia activates the herpes zoster virus.
W. G. Harding

686. **The Skeletal Lesions of Leucemic Children Treated with Aminopterin**
F. E. KARPINSKI and J. F. MARTIN. *Journal of Pediatrics* [*J. Pediat.*] **37**, 208–223, Aug., 1950. 8 figs., 11 refs.

The skeletal lesions were studied by radiography in a group of 35 children with acute leukaemia treated with "aminopterin". Serial chest films taken during the course of the therapy failed to show any regression of enlarged hilar nodes, pleural effusion, parenchymal infiltration and haemorrhage, passive hyperaemia, or pulmonary oedema.

Osteolytic lesions of the skull appeared only in 6 cases and were uninfluenced by aminopterin therapy. Lesions of the long bones were present in 81%, taking the form of osteolysis in 12 cases, subperiosteal formation of new bone in 11, and appearance of a transverse band of diminished density at the end of the shaft of the long bones in 22. Several types of lesion were frequently encountered together. An additional finding was the presence of transverse bands of increased density at the end of long bones, a feature observed in 5 of the cases during the course of aminopterin therapy. Their appearance was transient in nature and the bands became less prominent as the disease progressed. Disappearance of a true destructive bone lesion was observed in only one case treated with aminopterin. *R. Winston Evans*

687. **Chemotherapy of Leukemia. V. Effects of 2:4:6-Triethylenimino-s-triazine and Related Compounds on Transplanted Mouse Leukemia**
J. H. BURCHENAL, S. F. JOHNSTON, M. A. CREMER, L. F. WEBBER, and C. C. STOCK. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 708–712, Aug., 1950. 12 refs.

Forty-two compounds, of which 39 could be classed as triazines and 3 as ethylenimine ring compounds, were screened for chemotherapeutic activity against Ak4 mouse leukaemia. 2:4:6-Triethylenimino-s-triazine, 2:4-diethylenimino-6-amino-6-triazine, and hexamethylene diethylenurea significantly prolonged the survival time of the mice. The chemotherapeutic activity of the above compounds can probably be attributed to the ethylenimine structure. Four other compounds containing either a triazine or an ethylenimino moiety showed a slight chemotherapeutic effect.—[Authors' summary.]

688. **Anatomical Fundus Changes in Niemann–Pick's Disease.** (Die anatomischen Veränderungen des Augenhintergrundes bei der Niemann–Pickschen Krankheit)
H. DIDION. *Klinische Monatsblätter für Augenheilkunde* [*Klin. Mbl. Augenheilk.*] **116**, 131–135, 1950. 1 fig., 6 refs.

The eyes of uniovular twins who had the typical symptoms of Niemann–Pick disease were examined post mortem. Although these children were gentiles, the macula in life had shown a cherry-red spot with a surrounding grey-green ring. It was found that the red spot was due to the transparency of the foveola to light reflected by the choroid, which was absorbed in the rest of the macular region by the lipoid degeneration of the ganglionic cells, so that the parafoveal region appeared greenish. The histological picture was identical in the eyes of both twins, one of whom died 15 months before his brother, and demonstrated that the retinal degeneration is limited to the ganglion cells.

The author emphasizes that the red spot is not pathognomonic of any particular disease, but simply a symptom which may appear in advanced stages of Niemann–Pick disease. *S. S. B. Gilder*

689. **Primary Hodgkin's Disease of the Lung**
K. YARDUMIAN and L. MYERS. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 233–244, Aug., 1950. 6 figs., 13 refs.

In most cases Hodgkin's disease of the lung is secondary to lesions elsewhere. Here the authors describe a case in which they consider the primary lesion to have been in the lymph nodules in the parenchyma of the lung and submucosa of the bronchi. The patient was male, aged 52, and complained of fever and malaise, weakness, and a sore throat. His chest radiograph suggested chronic passive congestion due to cardiac disease or chronic bronchitis, pneumoconiosis, fungus infection, sarcoidosis, carcinomatosis, old tuberculous disease, or miliary tuberculosis. No diagnosis was made before death, which occurred a year after the first admission. At necropsy no palpable lymph nodes were found in the neck or axillary area; there was a right-sided pleural effusion. Macroscopically, the lung lesions resembled those of carcinoma. There were a few nodules of Hodgkin's disease in the liver. Microscopically, the alveoli and peribronchial spaces were filled in most parts of the lung with Hodgkin's tissue. *G. S. Crockett*

690. **Boeck's Sarcoidosis (Chronic Epithelioid-celled Reticulo-endotheliosis or Granulomatosis)**
S. J. LEITNER. *Tubercle* [*Tubercle*] **31**, 174–183, Aug., 1950. 4 figs., bibliography.

This paper from the Bernese Sanatorium at Leysin is essentially a short review of sarcoidosis in all its forms, with reference to the literature and to the findings in 38 of the author's own cases in Leysin and Berne. The term "sarcoidosis" is now applied collectively to a number of different conditions which, until the underlying common histology of the lesions was recognized, were formerly regarded as separate diseases. The first histological change is to be found in the lymph nodes and consists in a widening of the lymphoid sinuses and hyperplasia of the reticulum cells with subsequent formation of epithelioid cells. Later the reticulum fibres hyalinize and areas of coagulation necrosis appear, but caseation characteristically does not occur. The most commonly affected organs are the lymph nodes and the lungs, but the spleen, eyes, liver, kidneys, skin, bones, heart, and meninges may also be involved, in that order of frequency. Eosinophilia, monocytosis, hyperglobulinaemia, and hypercalcaemia are other incidental findings. The tuberculin reaction is positive in one-third of cases.

Tuberculin, gold, calcium, and ultraviolet light have been used in treatment without success. Radiotherapy is considered harmful because of the possibility of reactivation. In the author's opinion streptomycin, *para*-aminosalicylic acid, and thiosemicarbazone should be reserved for cases where there is also acute tuberculosis: in 3 of his own cases treatment with calciferol was disappointing in its results. He favours the view that the disease is an atypical form of tuberculosis.

Donough O'Brien

ANAEMIA

691. **Refractory Hypochromic Anaemia and Steatorrhoea. Treatment with Intravenous Iron**
C. F. HAWKINS, A. L. P. PEENEY, and W. T. COOKE. *Lancet* [*Lancet*] **2**, 387–391, Sept. 23, 1950. 7 figs., 13 refs.

Six cases of hypochromic anaemia associated with steatorrhoea, which were refractory to oral therapy with iron, responded to intravenous therapy. The authors' criteria for describing an anaemia as refractory to iron by mouth are: (1) A potent preparation of iron must have been used. (2) Full doses must have been taken and tolerated for an adequate period. (3) The presence of haemorrhage, chronic infection, renal failure, and hypoplasia must have been excluded.

The patients studied were known to have taken 10 gr. (0·65 g.) ferrous sulphate 3 times a day for at least 8 weeks without improvement. They all responded to "ferrivenin" given intravenously in doses of 20, 60 and then 100 mg. (100 mg. = 5 ml.) at intervals of 24 hours to 3 days until the required total dosage was reached. They have been under observation for from 6 to 18 months, and so far no further iron has been necessary. Striking features were the rapid improvement in the mean corpuscular haemoglobin concentration and the pronounced increase in the mean cell volume associated with obvious macrocytosis in 5 out of 6 cases.

The authors suggest that a high proportion of patients with refractory iron-deficiency anaemia will be found to have steatorrhoea if fat-balance tests are performed [a suggestion which fits well with the experience of other clinics]. *Janet Vaughan*

692. **Addisonian Pernicious Anaemia. Confirmatory Evidence of a Factor Inhibiting Erythropoiesis**
B. R. THOMPSON. *Clinical Science* [*Clin. Sci.*] **9**, 281–285, 1950. 7 refs.

At the Royal Victoria Infirmary, Newcastle-upon-Tyne, bone-marrow cells, obtained by aspiration from cases of pernicious anaemia in relapse, were cultured in media containing varying proportions of blood plasma or serum derived from normal subjects and from patients with pernicious anaemia. The method of culture used was that of Osgood and Brownlee and erythroblasts were classified according to the method of Davidson *et al.* (*Quart. J. Med.*, 1942, **11**, 19).

Cultures in various dilutions of normal plasma ranging from 10 to 100% showed no significant difference in the degree of maturation. But in cultures made in media containing plasma from cases of pernicious anaemia the number of immature cells present increased with the concentration of plasma present, though this effect varied with different samples of plasma. Moreover, the addition of pernicious-anaemia plasma to normal plasma produced an inhibition of the maturing effect of the latter. These findings agree with those of Rusznyak *et al.* (*Hungarica Acta med.*, 1948, **1**, 1) who suggested that such an inhibitory factor was present in the serum of patients suffering from pernicious anaemia, and that the disease was not simply due to the absence of a specific maturation element. *A. T. Macqueen*

693. **Megaloblastic Anemia of Pregnancy: Response to Pteroylglutamic Acid after Failure of Response to Liver Extract and Vitamin B_{12b}**
V. GINSBERG, J. WATSON, and H. LICHTMAN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 238–241, Aug., 1950. 1 fig., 12 refs.

A case of megaloblastic anemia of pregnancy is presented which failed to respond to refined liver extract and vitamin B_{12b} and which then responded maximally to pteroylglutamic acid.—[Authors' summary.]

694. **Studies on the Relationships of Vitamin B_{12}, Folic Acid, Thymine, Uracil, and Methyl Group Donors in Persons with Pernicious Anemia and Related Megaloblastic Anemias**
R. W. VILTER, D. HORRIGAN, J. F. MUELLER, T. JARROLD, C. F. VILTER, V. HAWKINS, and A. SEAMAN. *Blood* [*Blood*] **5**, 695–717, Aug., 1950. 12 figs., 42 refs.

The authors treated with folic acid 42 patients suffering from pernicious anaemia. They were given 30 mg. three times weekly over periods of 2 to 3 years, and 36 have been under regular observation. Of these, 11 have

remained in a satisfactory condition, 4 have died, 5 have had haematological relapses, 7 have had severe neurological relapses, and 9 both haematological and neurological relapses. The haematological relapses gave place to satisfactory remissions when the patients were given liver extract or thymine; some showed partial improvement with increase in dosage of folic acid, but this was followed by further relapse within a few months, when subsequent response to liver extract or vitamin B_{12} was retarded. Subacute combined degeneration of the cord or peripheral neuritis developed in every patient with pernicious anaemia who received increasing doses of folic acid in order to maintain haematological remission. It is thought that folic acid exerts its effect by "mass action"; it either is essential for the formation of thymine and other pyrimidines and purines or facilitates the utilization of these substances. Folic acid, by pushing some chemical reaction to completion in the face of a deficiency of vitamin B_{12}, probably depletes the supply of this latter factor and leads to development of neurological changes.

The suggestion that uracil may be a precursor of thymine is made, based on the haematological responses produced in 2 out of 3 patients with pernicious anaemia treated with 15 to 30 g. of uracil daily. A patient with macrocytic anaemia of pregnancy which failed to respond to uracil gave partial responses to choline and methionine, and complete response to thymine. Choline and methionine may supply the methyl groups for the formation of thymine. In these cases an activating substance may be necessary for this methylation process.

The authors refer to a previously reported case of megaloblastic anaemia refractory to liver extract and vitamin B_{12}, but responding to folic acid; the condition was probably not due to a folic-acid deficiency, for the latter was excreted in the urine, and it is possible that the "Wills factor" was deficient. This factor and folic acid may correspond to the activators of the above methylation reaction.

They suggest that folic acid, liver extract, and vitamin B_{12} are necessary for the formation of nucleic acid and nucleoprotein, and that the megaloblast, which is common to pernicious anaemia and related macrocytic anaemias, is a primitive erythroblast with an abnormality of nucleoprotein metabolism. The so-called maturation arrest in marrow elements thus occurs because of this abnormality induced by a deficiency of vitamin B_{12}, folic acid, the "Wills factor", and other chemical activators.

John F. Wilkinson

695. **Effect of Vitamin B_{12} on Neuropathy in Pernicious Anaemia Treated with Folic Acid**
H. FULD. *British Medical Journal* [*Brit. med. J.*] **2**, 147–148, July 15, 1950. 6 refs.

696. **The Significance of ABO Compatibility and its Relationship to the Intensity of Rh Immunization**
S. P. LUCIA and M. L. HUNT. *Blood* [*Blood*] **5**, 767–772, Aug., 1950. 11 refs.

The serological findings in 1,337 obstetric cases at the University of California Hospital are analysed, the cases being those in which the ABO blood group and Rh characteristics of mother and child were known, selected from a total of 11,649 obstetric cases over a 6-year period. Among these 1,337 patients were 170 Rh-negative women whose blood contained 2+ or more of Rh antibodies. Of the whole series, 45% were of blood group O and 39% of group A, whereas the corresponding figures for the 170 sensitized women were 33 and 54%. Of the cases in which the infant developed haemolytic disease the ABO blood groups of the mother and child were compatible in 95%, compared with 80% in the unaffected cases. The incidence of both erythroblastosis and compatibility was highest when the mother was of group A. In Rh-negative women who did not become sensitized after a fifth pregnancy compatibility was less common than in those who did. The conclusion is drawn that sensitization of Rh-negative women is more likely to occur where there is ABO compatibility between mother and infant.

G. Jacob

697. **Attempts at Desensitization of Women Immunized by the Rh Factor. I. The Use of Ethylene Disulfonate**
W. C. MOLONEY. *American Journal of Obstetrics and Gynecology* [*Amer. J. Obstet. Gynec.*] **60**, 616–625, Sept., 1950. 2 figs., 8 refs.

In this paper some of the difficulties in evaluating methods of prevention of hemolytic disease in the newborn have been pointed out. Suggestions as to criteria for the selection of clinical material for such studies have been outlined. Observations are reported on a series of Rh-negative pregnant women, iso-immunized to the Rh factor, given ethylene disulfonate in 10 cases and distilled water in 2 cases. Of the infants of 10 women treated with ethylene disulfonate, one survived following an exchange transfusion, 3 were Rh negative and escaped hemolytic disease, and 6 failed to survive. Only 2 women were treated with distilled water instead of ethylene disulfonate and both infants died. From the experience in this series of cases it is concluded that ethylene disulfonate exerts no influence on antibody production due to Rh iso-immunization, and that this drug does not prevent hemolytic disease of the newborn. —[From the author's summary.]

See also Sections Pharmacology and Therapeutics, Abstract 482; Paediatrics, Abstract 617.

HAEMORRHAGIC DISEASES

698. **Rutin Therapy in Diffuse Capillary Bleeding: Ineffectiveness when Fragility Tests are Normal**
W. H. GLASS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220**, 409–413, Oct., 1950. 11 refs.

The treatment of hereditary haemorrhagic telangiectasia includes blood transfusion, the use of snake venom, and fulguration of bleeding points. As the condition is characterized by spontaneous variations in the appearance of the lesions and in the amount of bleeding, systemic medication is advisable in the management of the disease. Kushlan (*Gastroenterology*, 1946, **7**, 199) reports excellent results from the administration of rutin

in doses of 60 to 100 mg. daily, improvement being recorded within 24 hours. From his own experience, however, the present author doubts whether the treatment is of any value. In 5 cases of the disease daily doses of rutin ranging from 60 to 150 mg. were administered intermittently for 2 to 3 years. No objective evidence was obtained as to the efficacy of the treatment, but 2 patients were under the impression that the tendency to bleed had been controlled to some extent.

The first patient in the series was a man aged 47 years with multiple areas of telangiectasia on the face. Even trivial injuries caused the nasal mucosa to bleed freely and epistaxis was often initiated by sneezing. Rutin was administered for 30 months, but the treatment failed to check recurrences of epistaxis. This patient's brother and a cousin also suffered from the disease and a similar lack of objective success attended the same treatment in these and 2 other, unrelated, patients. In contrast, a good response was obtained in a woman aged 51 years with diffuse capillary permeability of unknown origin. A prolonged course of treatment with ascorbic acid had been ineffective. Treatment with rutin, however, reduced the tendency to bruise. There was a pronounced diminution in the Göthlin index and in the erythrocyte sedimentation rate. Care was taken not to administer sulphonamides, because these compounds are believed to exert an adverse effect on the action of rutin.

A. Garland

699. **The Treatment of Hereditary Haemorrhagic Telangiectasia with Rutin and Ascorbic Acid.** (Le vitamine P e C nel trattamento del morbo di Rendu-Osler)

M. BALDUINI and G. BERTOLOTTI. *Acta Vitaminologica* [*Acta vitamin., Milano*] **4**, 156–161, Aug., 1950. 1 fig., bibliography.

The treatment with rutin of a family suffering from hereditary haemorrhagic telangiectasia is described in this paper. The mother and 3 of her 4 sons had had frequent, though not very severe, haemorrhages, mostly from the nose, since their early childhood. Complete haematological investigation, including bone-marrow puncture, was carried out in each case. The bleeding time was in all 4 cases slightly or moderately prolonged, the coagulation time was prolonged in 2 of the sons, and there was a reduction in the platelet count of the 3 affected sons (70,000, 80,000, and 120,000 per c.mm. respectively) but not of the mother. The fourth son, who had never shown any haemorrhagic tendencies, had a completely normal blood picture.

The bleeding time and coagulation time, as well as the platelet count, became normal within 3 to 8 weeks after treatment started. In the case of the mother 60 mg. rutin was given daily. Because of age differences, the sons received 80, 60, and 25 mg. rutin, and in addition 100, 75, and 25 mg. ascorbic acid daily. During one year of observation no treated patient had any haemorrhagic manifestations.

[This is another important contribution to the treatment of hereditary haemorrhagic telangiectasia with rutin. Unfortunately the authors identify rutin with vitamin P in this paper. Owing to the confusion caused by identification of "vitamin P" with one or another of the group of polyphenolic substances, the Federation of American Societies for Experimental Biology adopted a resolution recently "that the term vitamin P should no longer be employed".] *Z. A. Leitner*

700. **Study of a Case of Purpura Associated with Bone Changes and Formation of a Gel in the Serum on Cooling**

H. C. LUCEY, E. LEIGH, H. HOCH, J. R. MARRACK, and R. G. S. JOHNS. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **31**, 380–389, June, 1950. 1 fig., 27 refs.

A farm-labourer of 57 complained of blood spots in his skin and swellings over the bones of his legs, pains in his leg bones, and occasional small haemoptyses. Later he noticed mistiness of vision, whose disappearance was followed by transient enlargement of his salivary glands. Radiographic examination showed increased density and coarse trabeculation of the whole skeleton, with marked thickening of the cortex of the long bones. The general picture was much like that in Paget's disease, but the alkaline-phosphatase level in serum was only slightly raised; the alternative diagnosis was sarcoidosis. No evidence of myelomatosis could be obtained.

The patient's serum formed a gel on cooling; it passed from fluid at 27° C. through cloudiness at 25° C. and increased vicosity at 24° C. to the formation of a solid gel at 23° C.; the whole process was reversible. The active component was a substance migrating electrophoretically with the β globulin, but it cross-reacted with anti-γ-globulin sera. It contained 0·5% cholesterol, less than 0·03% lipid phosphorus, 7% or less total lipid, and about 5·8% carbohydrates (as galactose-mannose). Its sedimentation constant was $17{\cdot}2\times10^{-13}$, corresponding to a molecular weight between 400,000 and 1,000,000. The tyrosine : tryptophan ratio (1·63 : 1) was lower than that found in β or γ globulin, or in fibrinogen. The protein is compared with that obtained from cases previously described, and the symptoms shown by the patients are contrasted. *C. L. Oakley*

701. **Febrile Thrombopenic Purpura with Hemolytic Anemia and Platelet Thrombosis**

P. T. GOLDENBERG, J. E. THAYER, and L. P. HASTINGS. *New England Journal of Medicine* [*New Engl. J. Med.*] **243**, 252–256, Aug. 17, 1950. 3 figs., 15 refs.

Several cases of the syndrome of fever, progressive anaemia, mild icterus, thrombopenia, and changes in the central nervous system have now been reported in the literature. The case reported in this paper was unusual because the onset took the form of a confusional state, for which the patient was admitted to a mental hospital. The usual manifestations of haemorrhage, especially from the vagina, severe anaemia, and constant pyrexia appeared very soon. As in other cases, there was no response to transfusion and the patient died about 3 weeks after the onset. Post-mortem examination showed numerous thrombi in the blood vessels of almost every organ, including the brain. These thrombi were made up of masses of platelets, and none of the usual fibrin

was present. This finding also agrees with previous descriptions. The literature and theories of aetiology are fully discussed. *M. C. G. Israëls*

HAEMATOPOIETIC SYSTEM

702. **The Role of the Hypophysio-hypothalamic System in the Pathogenesis of Erythraemia and Symptomatic Polycythaemia.** (A hypophysis-hypothalamus rendszer szerepe a polycythaemia vera és a polyglobuliák pathogenesisében)
I. HAYNAL, F. GRÁF, J. MATSCH, M. CSELEY, and S. EGEDY. *Orvosi Hetilap* [*Orv. Hetil.*] **91**, 1025–1034, Aug. 20, 1950. 5 figs., bibliography.

There appears to be ample clinical and experimental evidence for the central nervous and hormonal regulation of erythropoiesis. Various pathological conditions affecting the pituitary and hypothalamic regions are not infrequently accompanied by erythraemia. In order to assess the part played by the pituitary–hypothalamic system in the pathogenesis of polycythaemia vera, the following estimations were carried out in 10 cases of erythraemia: sugar tolerance, insulin and adrenaline blood sugar curves, adrenaline blood-pressure curve, antidiuretic, vasopressor, and blood-sugar-elevating properties of the cerebrospinal fluid on injection into cats and rats, basal metabolic rate, specific dynamic action of protein, serum cholesterol, sodium, and potassium levels, and the size of the sella turcica as estimated radiologically. In 8 of the patients the results of the tests suggested increased anterior pituitary function. This could also be demonstrated in cases of symptomatic polycythaemia. Treatment with aneurin, sex hormones, and deep *x* rays, which are believed to decrease pituitary function, failed to influence the blood condition appreciably, although the functional tests revealed diminution of pituitary function as a result of treatment. It is nevertheless concluded that the increased erythropoiesis in polycythaemia is in some way connected with hyperfunction of the pituitary–hypothalamic system.
E. Nassau

703. **Polycythaemia Vera Co-existing with Malignant Tumours (Particularly Hypernephroma).** [In English]
A. VIDEBÆK. *Acta Medica Scandinavica* [*Acta med. scand.*] **138**, 239–245, 1950. 23 refs.

The relations of polycythaemia to Cushing's syndrome and hypercorticoidism and to intracranial tumours are reviewed, and 2 cases of polycythaemia coincident with hypernephroma, described by other authors, are mentioned. Three cases are reported. The first patient was a man who had polycythaemia with haematuria, and received courses of *x*-ray therapy to the long bones with temporary remissions. At necropsy 13 months after the first episode of haematuria, hypernephroma with pulmonary metastases was found. The second patient, a woman, had signs of polycythaemia for 5 years, before haematuria, pain, wasting, and haematemesis led to death. Necropsy revealed a metastasizing hypernephroma. The third patient, a female, had haematuria and the blood picture of polycythaemia, with an *x*-ray finding of defect in the right kidney. Nephrectomy was performed for a hypernephroma. The evidence from the cases of polycythaemia seen by the author does not suggest an increased susceptibility to malignant growth, apart from leukaemia, in polycythaemia. *E. H. Johnson*

704. **Multiple Myeloma**
E. G. BROWNELL. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **63**, 157–163, Aug., 1950. 2 figs., 22 refs.

During a period of 3 years, 21 cases of multiple myeloma were investigated at the Winnipeg General Hospital. The patients' ages ranged from 45 to 84 years, 11 of the 21 being between 50 and 64. Loss of weight and pain in the back were common complaints. A tumour was observed in 3 cases, being situated in the region of the left clavicle, the jaw, and the ilium respectively. In another case sciatic pain was produced by tumour formation in the vicinity of the sciatic nerve. A few patients had atypical manifestations such as refractory anaemia, painless arthropathy, and macroglossia due to amyloidosis. Abnormal bleeding, associated with hyperglobulinaemia in 3 out of 4 cases, was also observed, 2 patients suffering from epistaxis and 2 from rectal bleeding. One patient had a subdural haematoma.

Examination of the blood showed anaemia, an increase in the erythrocyte sedimentation rate, rouleaux formation, and myeloid immaturity. In 6 cases the peripheral blood contained plasma cells. Aspiration of the sternal marrow was carried out in 17 cases and was found to be of diagnostic value. As plasma cells were detected in every instance, the author is in agreement with Diggs and Sirridge (*J. Lab. clin. Med.*, 1947, **32**, 167), who consider that the " myeloma cell " is a young plasma cell.

The biochemical changes found included hyperproteinaemia and hypercalcaemia. In 12 cases the blood globulin level was above 4 g. per 100 ml., and in 4 cases the serum calcium content amounted to more than 12 mg. per 100 ml. Bence-Jones proteinuria was detected in only 3 cases, but albuminuria occurred in 15. In 10 cases radiological findings were positive, especially in the spine; in 5 cases punched-out osteolytic lesions, and in 5 cases osteoporotic changes, were seen. Death occurred in 17 cases at an average interval of 12·7 months after the onset of symptoms. *A. Garland*

705. **Reactions of the Bone Marrow in Kidney Disease. The Mechanism of Disturbance of Haematopoiesis.** (Типовые реакции костного мозга при заболеваниях почек. Механизм нарушения костномозгового кроветворения)
G. I. ALEKSEEV. Терапевтический Архив [*Terap. Arkg.*] **22**, No. 4, 58–65, July–Aug., 1950. 13 refs.

Renal disease may be accompanied by abnormal counts of bone-marrow cells. In acute nephritis and in hypertension there may be a large proportion of erythroblasts. In hypertension, as in chronic nephritis, there may be marrow hypoplasia, and macroblastosis may occur in chronic nephritis. *Jeffrey Boss*

Respiratory Disorders

706. **Telangiectasis of the Lungs, with Two Case Reports of Hereditary Haemorrhagic Telangiectasia with Cyanosis**
A. J. BRINK. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **19**, 239–249, July, 1950. 2 figs., 27 refs.

Both the cases of pulmonary telangiectasis reported were investigated with a view to determining the cause of the cyanosis. In the first case, that of a young woman, an angiomatous condition of the liver had been found at laparotomy, and during the period of observation angiomata in skin and mucous membranes increased in size and number. The cyanosis also increased but was relieved by oxygen; radiological, electrocardiographic, angiocardiographic, and blood gas analyses excluded a congenital cardiac defect and indicated the pulmonary origin of the cyanosis. Since hepatic and skin angiomata were present, it seemed reasonable to postulate the existence of minute arterio-venous shunts in the lungs sufficient in number to result in imperfect oxygenation of the blood.

The second patient was a woman in late middle age with increasing cyanosis and dyspnoea, partly relieved by oxygen, who had a small number of cutaneous and mucosal telangiectases and a loud bruit below the angle of the left scapula; radiologically the large, tortuous, pulsatile shadow of an arterio-venous fistula was visible. It is noted that cyanosis is unusual in the Rendu–Osler–Weber syndrome, but it is considered that, in a pathological process of which the most prominent feature is telangiectasia, structures such as the physiological broncho-pulmonary anastomotic channels may well increase in size and number. *W. S. Killpack*

707. **Artificial Pneumoperitoneum in the Treatment of Pulmonary Emphysema. A Preliminary Report**
R. H. FURMAN and J. J. CALLAWAY. *Diseases of the Chest* [*Dis. Chest.*] **18**, 232–243, Sept., 1950. 5 figs., 10 refs.

Artificial pneumoperitoneum as a method of treating pulmonary emphysema, although first introduced in 1924, has not hitherto been widely used. The authors here describe, in a preliminary report, 5 cases in which it has been usefully employed. It is an extension of the older form of treatment by abdominal binder and belt and is directed towards raising and mobilizing the low, fixed diaphragm, thus reducing the residual air, increasing the vital capacity, and so greatly assisting the gaseous exchange. Carbon dioxide retention and anoxaemia are the principal biochemical changes in emphysema.

In the 5 cases reported the position of the diaphragm on inspiration and expiration was studied fluoroscopically before and after the induction of pneumoperitoneum. Exercise tolerance was estimated by means of the Master 2-step test, a Millikan oximeter being used to measure the oxygen saturation of arterial blood, and the results equated with changes in the vital capacity. The latter was measured over a period of expiration limited to 3 seconds, because prolonged expiratory effort may enable emphysematous patients to reach almost normal values. The initial injection of air varied in volume between 400 and 1,200 c.cm., and was followed by refills at intervals of 3 days, 4 days, and finally of one week, a final pressure of 12 cm. water being aimed at. [In this the authors have probably been more thorough and persistent than most who have used this form of treatment.]

From the case histories given, the improvement both in the test results and the clinical condition appears to have been quite definite. In one case it was 3 months before improvement started, but in another it was immediate: generally it was early. The vital capacity increased by 500 to 1,000 c.cm. in each case. Where asthma had been associated there was a startling reduction in the number of attacks. The treatment was tried in 2 additional cases, but had to be stopped because severe chest and shoulder pain occurred. Chronic infection of the lung bases and diaphragmatic adhesions were the complicating factors in these cases. The authors finally discuss briefly the contraindications and complications of this procedure and urge its further and more widespread trial in cases of emphysema. [Pneumoperitoneum undoubtedly appeared to have proved a valuable symptomatic therapeutic agent in their hands.] *Ronald S. McNeill*

708. **Severe, Sporadic Virus Pneumonias. Diagnostic and Therapeutic Problems**
H. A. REIMANN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 81–85, Sept. 9, 1950. 5 figs., 16 refs.

The author describes 7 cases of severe sporadic pneumonia of presumed virus aetiology. The clinical picture was indistinguishable from that seen in the epidemic form of virus pneumonia. No causative organisms could be demonstrated. Cold agglutinins were present in one case only. In 4 patients complement-fixation tests were found to be negative for one or more of the viruses known to cause pneumonia. [Serological investigations were not carried out in all cases.] *J. R. Bignall*

709. **Acute Primary Klebsiella Pneumonia**
M. NATARO, D. SHAPIRO, and A. T. GORDON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 12–16, Sept. 2, 1950. 3 figs., 19 refs.

The authors have treated 5 patients with pneumonia due to *Klebsiella pneumoniae* (Friedländer's bacillus), 4 with streptomycin and one with aureomycin. Of the streptomycin-treated patients 3 recovered slowly and the fourth died; the patient receiving aureomycin recovered rapidly. Ten other published cases of streptomycin-treated klebsiella pneumonia are reviewed. The over-

all mortality in these 14 cases was 20%, which compares favourably with previously reported mortality of 50 to 97% in similar cases treated with sulphonamides and penicillin. The authors found that with streptomycin treatment the incidence of subsequent pulmonary fibrosis diminished. They therefore conclude that streptomycin is an effective drug in this disease.

Aureomycin has apparently not been used before for klebsiella pneumonia. Its dramatic effect in the one case reported here suggests that it deserves further trial.

John R. Forbes

710. **Smoking and Carcinoma of the Lung. Preliminary Report**

R. DOLL and A. B. HILL. *British Medical Journal* [*Brit. med. J.*] **2**, 739–748, Sept. 30, 1950. 2 figs., 10 refs.

The Registrar-General's figures show that from 1922 to 1947 the annual number of deaths from carcinoma of the lung in England and Wales increased from 612 to 9,287, an increase out of all proportion to the increase of the population. Between 1921-30 and 1940–44 the male death rate from this condition at the ages of 45 and over increased six-fold, the female about three-fold.

It is hard to believe that improved diagnosis is solely responsible for the increase. Two main causes have been suggested: tobacco smoking, and general atmospheric pollution from a variety of sources. The significance of the former was particularly investigated by the authors, who have drawn their material from 20 London hospitals.

The aim of their investigation was to determine whether patients with carcinoma of the lung differed materially from other persons in respect of their smoking habits. Patients with carcinoma of the stomach, colon, and rectum were also incorporated in the inquiry. Each patient was interviewed by one of four almoners, who used a set questionary. They also made similar inquiries from a group of " non-cancer control " patients. The diagnosis of each patient was checked after discharge from, or death in, hospital, in all but nine instances (0·4% of the total).

There were 1,732 patients presumed at interview to be suffering from carcinoma of lung, stomach, or large bowel, and 743 general medical and surgical patients as controls; 709 patients with carcinoma of the lung were interviewed, and of these 60 were women. These 709 patients were carefully compared with 709 control patients with diseases other than cancer of the lung, deliberately selected to be closely comparable in age and sex.

The assessment of smoking habits is not easy, because individuals vary in the amount of tobacco smoked. Patients were particularly asked: (1) if they had smoked at any period in their lives; (2) the ages at which they had started and stopped; (3) the amount they were in the habit of smoking before the onset of the illness which had brought them into hospital; (4) the main changes in their smoking history and the maximum they had ever been in the habit of smoking; (5) the varying amount smoked in pipes and cigarettes; (6) whether they inhaled. A smoker was finally defined as a person who had smoked one cigarette a day for as much as one year. In order to check the veracity and accuracy of the patients' memories, 50 unselected control patients with disease other than cancer were interviewed a second time 6 months or more later. The results obtained showed that the detailed smoking histories obtained were reliable enough to indicate general trends and to substantiate material differences between groups. The table shows the proportion of smokers and non-smokers in patients with lung carcinoma, and in control patients.

Disease Group	No. of Non-smokers	No. of Smokers	Probability Test
Males:			
Lung-carcinoma patients (649)	2 (0·3%)	647	P (exact method) =0·00000064
Control patients with disease other than cancer (649)	27 (4·2%)	622	—
Females:			
Lung-carcinoma patients (60)	19 (31·7%)	41	$\chi^2=5{\cdot}76$; n=1 $0{\cdot}01<P<0{\cdot}02$
Control patients with disease other than cancer (60)	31 (53·3%)	28	—

The striking feature is the very small proportion of non-smokers with carcinoma of the lung. Analysing the amount of tobacco smoked by the individual the authors find that in the lung-carcinoma group 26% of the male patients fall in the two highest-consumption groups (25 cigarettes a day or more), while in the control group the figure was only 13·5%. A similar trend was observed for women, but the numbers involved were rather smaller. Further tables estimating the maximum amount of tobacco ever consumed regularly, the total amount of tobacco ever consumed by smokers, and the age of starting to smoke, the number of years of smoking, and number of years without smoking were also drawn up; they all show a significant and clear relation between smoking and carcinoma of the lung.

An attempt was made to assess the relative importance of pipe and cigarette smoking. Of 525 lung-carcinoma patients who had smoked either pipes or cigarettes, but not both, 5·7% were pipe smokers; of 507 control patients 9·7% were pipe smokers. Statistical analysis shows that the lower proportion of pipe smokers and the corresponding excess of cigarette smokers in the lung-carcinoma groups was unlikely to be due to chance, and the authors conclude that pipe smoking is less related to carcinoma of the lung than is cigarette smoking.

The inhalation of tobacco smoke was investigated, 61·6% of 688 lung-carcinoma patients of both sexes stating that they inhaled; of 650 control patients 67·2% inhaled. The difference is not statistically significant.

The authors conclude that: (1) there is a real association between carcinoma of the lung and smoking; (2) there is no association between smoking and other respiratory diseases, or between smoking and cancer of the other sites (mainly stomach and large bowel). They also show that the risk of developing carcinoma of the

lung increases steadily as the amount smoked increases. They comment on the anomalous finding of inhaling. No evidence of the nature of the carcinogen was found, and they point out that arsenic is the only carcinogenic substance that has been found in tobacco smoke. This raises the possibility that the tobacco itself is not to blame, and that the source of the arsenic might be various insecticides used in tobacco cultivation.

[This very important and long article should be read in the original.] *Maxwell Telling*

711. **The Diagnosis of Bronchial Carcinoma.** (Sur le diagnostic du cancer du poumon)
E. HUIZINGA. *Annales d'Oto-Laryngologie* [*Ann. Oto-laryng.*] **67**, 395–402, May–June, 1950. 4 figs.

The author gives a short account of 110 cases of bronchial carcinoma observed during the past 5 years. Bronchoscopy and bronchography were used as diagnostic procedures, the latter preceding the former. Biopsy examination gave a positive result in 80% of cases. Bronchography was employed to locate lesions inaccessible to the bronchoscope. Removal of tissue for biopsy was carried out blindly by a small curette, in 14 cases with positive results. It is claimed that bronchography often reveals abnormalities, such as compression or an enlargement of the carina, which have some bearing on operability. Cases and radiographs are discussed which illustrate the value of the procedure.

The results of cytological examination of bronchial secretions, as advocated by Clerf, are inconclusive and mistakes are easily made. If, however, a cytological examination reveals the presence of suspicious-looking cells in a case in which the radiograph shows a pulmonary shadow, the indications for operation become more clearly defined. *E. D. Dalziel Dickson*

712. **Early Detection of Bronchogenic Carcinoma**
R. R. SHAW. *Diseases of the Chest* [*Dis. Chest*] **18**, 185–197, Sept., 1950.

The first successful operation of removal of a lung for bronchogenic carcinoma was performed by Graham 16 years ago. Since then the operative mortality has fallen from 50 to 10%, but the over-all salvage rate in the disease remains disappointingly low. The author bases his paper on a survey of 210 cases of bronchogenic carcinoma seen over a period of 3 years. Only 25% were suitable for surgical resection and in these there was an operative mortality of 6% which, in view of the age of the patients and difficulties of the operation, is a figure that could not easily be lowered. In 25% of cases the initial complaint for which the patient consulted his doctor was one indicating inoperability in that it was due to extension of the growth to organs other than the lung. Moreover, approximately 20% of all the tumours were of the undifferentiated type, which invariably turns out to be inoperable, so that the author estimates that, allowing for overlapping of these two groups, 40% of his cases were inoperable from the start. In general there was a delay of approximately 5 months between the onset of symptoms and the first visit to a physician, and a further 6 months before a correct diagnosis was made. The most common initial diagnoses were " virus pneumonia " and " unresolved pneumonia ".

In bronchogenic carcinoma the first change is in the bronchial mucosa, and the resulting bronchial obstruction first shows itself by a localized wheeze and emphysema. Change in the character of the cough to the paroxysmal type and early streaking of the sputum with blood is very important. Radiography is still the most valuable method of detection, but early cases may be missed on mass radiography, unless repeated. Bronchoscopy may also fail to demonstrate lesions lying in the more peripheral and smaller bronchi. Sputum examination may be very helpful in diagnosis, but does not, of course, replace bronchoscopy or thoracotomy. Thoracotomy may be necessary for the diagnosis of an early case, and should certainly be carried out where there is sufficient evidence, even in the absence of histological proof. Increase in the salvage rate in this important disease, which is now the most common type of carcinoma causing death in males, depends to a great extent on early and accurate diagnosis by the general practitioner. *Ronald S. McNeill*

713. **Epidemic of Benign Dry Pleurisy**
D. G. H. SYLVESTER. *British Medical Journal* [*Brit. med. J.*] **2**, 653–655, Sept. 16, 1950. 17 refs.

The author, working at St. Mary's Hospital, London, describes an epidemic of benign dry pleurisy occurring in two nearby households. The main symptom was pain of sudden onset in the upper abdomen, costal margin, and shoulders, worse on coughing or lying down and lasting for 3 to 4 days. Pyrexia and transient pleural friction were present in 2 cases observed. Leucocyte counts were normal. In one case the erythrocyte sedimentation rate was raised and there was decreased translucency of one lung base. Five months later sera from 5 of these cases gave positive complement-fixation reactions to the Coxsackie-2 strain of virus. The first cases in both households were in food handlers; this suggests an alimentary spread at the onset, with droplet infection in the later cases owing to close proximity of living quarters. *I. Ansell*

714. **Pleural-fluid Eosinophilia**
F. G. MACMURRAY, S. KATZ, and H. J. ZIMMERMAN. *New England Journal of Medicine* [*New Engl. J. Med.*] **243**, 330–334, Aug. 31, 1950. 45 refs.

Three patients are described who had pleural effusions containing over 5% of eosinophil leucocytes. In one of these cases the condition followed lobar pneumonia, the second had " a background of allergic disease ", and the third was associated with Hodgkin's disease. Other conditions associated with eosinophilia in pleural effusion are listed from a survey of the literature. It is suggested that a pleural effusion with eosinophilia is unlikely to represent the first sign of tuberculosis, although eosinophilic effusions have been reported in association with established tuberculous disease of the lung.
D. A. K. Black

See also Section Hygiene and Public Health, Abstracts 444–5.

Digestive Disorders

STOMACH AND INTESTINES

715. **Disturbances of Enzyme and Acid Production in the Stomach; their Diagnostic Significance and their Treatment.** (Über Störungen der Fermen und Säureproduktion im Magen, ihre diagnostische Erfassung und therapeutische Beeinflussung)
R. MERTEN, H. RATZER, and U. KLEFFNER. *Deutsche Zeitschrift für Verdauungs- und Stoffwechselkrankheiten* [*Dtsch. Z. Verdau.- u. StoffwechsKr.*] **10**, 159–174, 1950. 6 figs., 25 refs.

Gastric juice contains a proteolytic ferment named cathepsin, which is active at a *p*H of 3 to 5. The secretion of free and combined acid, of pepsin, and of cathepsin was estimated in conventional test-meals with alcohol or caffeine, and also *in vivo*, with a 2% haemoglobin solution, buffered at a *p*H of 3·5, as test-drink. Secretion of cathepsin was estimated separately. All 4 substances were secreted in roughly parallel amounts, and the subjects could be divided into 3 groups with good, moderate, and poor secretion. The authors lay great stress on the importance of cathepsin as the main proteolytic ferment acting in persons with low or moderate secretion of acid. *In vitro* tests were performed on a large number of proprietary digestive preparations, the majority of which did not digest protein satisfactorily.

[The number of cases investigated, presumably large, and the actual proportions with the three degrees of secretion are not given; only sample curves are presented.] *H. K. Goadby*

716. **On the Chemotherapy of Carcinoma. II.** [In English]
S. OSATO. *Tohoku Journal of Experimental Medicine* [*Tohoku J. exp. Med.*] **52**, 181–194, May 31, 1950. 7 figs., 10 refs.

The possibility of treating mouse carcinomata with aldehydes has been investigated by Strong and by Boyland, with suggestive results. The results of treating 6 [alleged] cases of gastric cancer in human subjects with citral and citronellal are here described. Two of the patients had been operated upon and the diagnosis of gastric carcinoma was established histologically. In the remainder the diagnosis rested on clinical symptoms and radiological appearances. An emulsion of citronellal and cod-liver oil with 2% citral was given by mouth and by rectum: a 5% emulsion of citral was also injected in doses of 3 to 8 ml. The swellings ascribed to the tumours are said to have decreased considerably, radiological abnormality became less pronounced, and the patients recovered their former health.

[Unfortunately no clear evidence is brought forward that these patients were suffering from cancer, and the period of observation after treatment appears to have been short.] *G. M. Findlay*

717. **Hiatus Hernia. Analysis of Twenty-five Cases**
E. E. SIMMONS, R. S. LONG, H. B. HUNT, and R. C. MOORE. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 253–265, Aug., 1950. 6 figs., 11 refs.

In this review, only cases of hiatus hernia in which some of the stomach is in the thoracic cavity are considered. In aetiology, maldevelopment of the diaphragm and factors tending to raise the intra-abdominal pressure are stressed. No particular body build was associated with this condition, the sexes were affected equally, and the patients ranged in age from 22 to 71, although 92% were over 40. The condition may be symptomless, or symptoms of peptic ulcer, gall-bladder disease, carcinoma of the stomach, angina, or some lung disorder may be simulated. Epigastric pain, with regurgitation and vomiting, and a sense of fullness after meals, are common. There is usually anaemia with or without haematemesis or melaena. The patient may suffer from anaemia alone. The epigastric pain is made worse by reclining and is partially relieved by walking about. There is usually epigastric tenderness with muscle guarding. Diagnosis is made radiologically, the lesion being seen best in films taken with the patient supine and his head down. Carcinoma of the stomach appears to be commoner in these cases. The patient should be instructed to avoid rough food, chew the food well, remain upright after meals, and elevate the head of the bed at night if symptoms are then severe; antispasmodics and antacids are useful. Operation is rarely necessary. *G. S. Crockett*

718. **Glucose-tolerance Test in the Diagnosis of Dysfunctio Vegetativa Digestiva (Pre-ulcer Syndrome).** [In English]
Å. EDLÉN. *Acta Medica Scandinavica* [*Acta med. scand.*] **138**, 161–178, 1950. 7 figs., 21 refs.

Following observations that liver function, and especially the glucose tolerance curve, may be abnormal in peptic ulceration, the author suggested that glucose tolerance tests might be of use in the diagnosis of the pre-ulcer syndrome, a condition suggesting ulceration but in which radiological confirmation is absent.

Thirty-five suitable cases were accordingly investigated at the Central Hospital, Östersund, Sweden. In the test, 1 g. of glucose in 10 or 20% solution per kg. body weight was given to fasting patients with an empty bladder. Blood sugar in capillary blood was estimated half-hourly for 3 hours. The following criteria were used in deciding whether the curve was abnormal: (1) a maximum blood sugar level of over 180 mg. per 100 ml.; (2) an increase over the fasting level of over 65 mg. per 100 ml.; (3) glycosuria; (4) failure of the sugar level to return to the fasting level within 150 to 180 minutes.

Of the 35 patients 28 had abnormal curves and 7 normal. Of the latter, 3 were thought to have gastritis and 4 a pre-ulcer syndrome in spite of the normal curve.

Of the others, 3 were known to have a peptic ulcer and the remainder had the pre-ulcer syndrome.

All the cases of pre-ulcer syndrome were successfully treated with "gynergen", ½ to 1 tablet sublingually at the beginning of a meal, or dihydroergotamine, 5 to 20 drops three times a day 15 minutes before meals.

Donough O'Brien

719. **The Relief of Peptic Ulcer Pain by Tetraethyl Ammonium Chloride**

P. A. BINTER and T. J. RANKIN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **33**, 649–658, Sept., 1950. 14 refs.

The effect of the operation of vagotomy on peptic ulcer has stimulated research into the effects of drugs capable of depressing vagal activity. The authors used tetraethylammonium chloride especially for its effect on ulcer pain. The dose given was 500 mg. intramuscularly.

Out of 70 male patients with peptic ulcer 27 were selected for trial of the drug because of the severity of pain. Great relief from pain was obtained with the dose stated in every case. There were no serious side-effects, but marked hypotension is produced so that the patient must lie flat for at least one hour after the injection. It is not claimed that the drug cures ulcer, but that it is useful in controlling severe pain either during medical treatment or before surgical operation for peptic ulcer.

J. W. McNee

720. **Clinical Trial of Banthine in 100 Patients with Peptic Ulcer**

K. S. GRIMSON, C. K. LYONS, and R. J. REEVES. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 873–877, July 8, 1950. 12 refs.

This is a preliminary report from Duke University on the clinical use, in cases of peptic ulcer, of banthine, a quaternary ammonium compound which, when given orally, reduces gastric motility and secretion. Although reduction in volume and acidity of the gastric juice after administration of the drug occurs less frequently than after vagotomy, and although it prevents hyperacidity after the injection of insulin only occasionally and in large doses, the effects of banthine and of vagotomy on motility are equally consistent. A series of 100 patients with clinical and *x*-ray evidence of peptic ulcer were treated with 100 mg. of banthine every 6 hours, advised to stop taking antacids and all other medicines, and encouraged to return to work. If prompt relief did not occur, the dosage of banthine was increased to 600 mg. daily and the diet corrected. [Apparently the trial was started with banthine methachloride, but later the methabromide was substituted.] Patients were classified as: (A) cases of duodenal ulcer without conventional indications for surgery (38); (B) cases of gastric ulcer with conventional indications for operation (7); and (C) cases of duodenal ulcer with conventional indications for surgery (55). Complicating haemorrhage had occurred previously in varying proportions of cases in all three groups, but none occurred during the time of treatment with banthine.

In the majority of cases pain was completely eliminated with a dosage of 400 mg. daily and 93 patients have continued, or returned to, regular work. Since the need for further treatment could no longer be determined by the occurrence of pain, periodical examination by fluoroscopy and serial radiography was used as a guide to the assessment of progress. Only in 29 patients was an ulcer crater seen initially, and in 21 this disappeared during the course of treatment. Duodenal deformity was present initially in 88 cases; this deformity disappeared in 7 cases and remained unchanged in 35, the others showing varying degrees of improvement. Side-reactions included dryness of the mouth (at the outset of treatment, diminishing later), weakness of visual accommodation, occasional constipation, and decrease in the force of urination.

The authors conclude from this early trial that by the use of banthine surgical treatment may be avoided in most cases of peptic ulcer.

R. N. Johnston

721. **The Effect of Atropine on Certain Gastric Functions in Patients with Duodenal Ulcer**

B. F. GILL and J. S. JESSUP. *Gastroenterology* [*Gastroenterology*] **15**, 736-746, Aug., 1950. 25 refs.

The authors, using a dye-dilution technique, measured the rate of gastric secretion and pyloric evacuation in 6 human subjects with duodenal ulcer. After a control period of one week, 1·2 mg. of atropine sulphate was given orally every 4 hours for one week; the dose was then increased to 2·4 mg., and this was given for one week also. Gastric function was measured and it was found that the atropine sulphate had caused a diminution in the free and total acid production and a fall in the rate of gastric secretion and the rate of pyloric evacuation. The usual side-effects occurred.

[The assumptions inherent in the dye-dilution technique are critically analysed, but the authors consider that the method is adequate for comparative studies such as theirs.]

John Naish

722. **Relative Incidence of Gastric and Duodenal Ulcers**

E. M. BROOKE. *British Medical Journal* [*Brit. med. J.*] **2**, 560–561, Sept. 2, 1950. 3 refs.

723. **Lipophagic Intestinal Granulomatosis (Whipple's Disease). Clinical and Pathologic Study of Thirty-four Cases with Special Reference to Clinical Diagnosis and Pathogenesis**

K. PLUMMER, S. RUSSI, W. H. HARRIS, and C. M. CARAVATI. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 280–310, Aug., 1950. 8 figs., bibliography.

A review is given of 34 cases of lipophagic intestinal granulomatosis collected from the literature. The disease occurs predominantly in males from 40 to 60 years old, and often begins with several years of polyarthritis, which is transient and migratory. Some cases began with postprandial abdominal pain, distension, and diarrhoea; here it is only a matter of months before the full picture of the disease is manifest. There is no blood in the stools, which usually resemble those of steatorrhoea. There are signs of hypoadrenocorticalism with weakness, emaciation, and hypotension. The skin is usually mud-coloured and the abdomen doughy to

palpation; in a few cases abdominal masses are felt. There is usually an iron-deficiency anaemia, but no glossitis. Diagnosis may only be made by laparotomy or at necropsy, when lipogranulomatosis of the mucosa of the small intestine and mesenteric lymph nodes is found; polyserositis, verrucous endocarditis, and infarcted viscera may also be found.

Differential diagnosis is from pancreatic insufficiency ulcerative colitis, adrenocortical insufficiency, and sprue. Symptomatic sprue due to blockage of lacteals by lymphoma or tuberculosis may be extremely difficult to distinguish. It is suggested that Whipple's disease is due to an "exhaustion" adrenal cortical deficiency causing an upset in fat absorption and flocculation of fat in the lacteals, so that they become blocked.

G. S. Crockett

LIVER

724. **The Flocculation Tests in the Differential Diagnosis of Jaundice**

H. Ducci. *Gastroenterology* [*Gastroenterology*] **15**, 628–641, Aug., 1950. 31 refs.

At the University of Chile Medical School, Hospital del Salvador, Santiago, the author carried out the following tests on the serum in 361 cases of hepatogenous jaundice and 167 cases of extrahepatic jaundice (not including haemolytic anaemia): estimation of alkaline-phosphatase content, cephalin–cholesterol flocculation, thymol turbidity and flocculation, and colloidal-gold precipitation. The results are analysed statistically and it is concluded that the combination of serum alkaline-phosphatase estimation with one of the flocculation or precipitation tests is of the most help in diagnosis. Of the flocculation tests used there is some slight statistical evidence that the cephalin–cholesterol test is the most sensitive.

The author also investigated the resistance of serum from cases of obstructive jaundice to the precipitating action of gamma globulin. He was unable to establish the nature of the resisting factor, but concluded that its presence was not related to changes in serum protein components. *Walter H. H. Merivale*

725. **Salt Retention in Cirrhosis of the Liver**

A. V. N. Goodyer, A. S. Relman, F. D. Lawrason, and F. H. Epstein. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 973–981, Aug., 1950. 1 fig., 24 refs.

In an attempt to clarify the problem of kidney function in cases of hepatic cirrhosis with ascites, the fate of hypertonic saline injected intravenously into patients with a restricted salt and water intake was studied. In a control group of 2 patients with cirrhosis but no ascites, sodium excretion in the urine rose to 190 to 1,147 mEq. per minute, but in patients with ascites the range was 2·5 to 113 mEq. per minute. The rise in serum sodium content was the same in both groups. The mechanism for the excretion of administered salt thus appeared to be defective in the cirrhotic patients with ascites. These excreted less than 10% of injected sodium, compared with up to 50% in the controls. Glomerular filtration rate was generally normal. An increased tubular reabsorption of sodium is therefore presumed to occur in cirrhosis with ascites, the cause of this being undetermined. *C. L. Cope*

726. **Correlation of Clinical Features of Cirrhosis of Liver with Findings on Biopsy**

H. Popper, S. S. Waldstein, and P. B. Szanto. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **20**, 724–737, Aug., 1950. 8 figs., 37 refs.

The correlation of liver biopsy findings in cases of hepatic cirrhosis with the clinical and biochemical features is usually considered unreliable. This study of such correlation is based on the investigation of 70 patients with cirrhosis by needle biopsy of the liver and by a battery of liver function tests. Liver-cell damage was graded according to the method previously described by the same group (Popper *et al.*, *Amer. J. clin. Path.*, 1949, **19**, 710).

The authors found that clinical and biochemical evidence of activity was most closely correlated with the degree of liver-cell damage, and less closely with evidence of focal necrosis and leucocytic reaction in the portal triads. Conversely, the degree of liver-cell damage showed the closest correlation with the intensity of the jaundice and with clinical and biochemical evidence of activity. Alcoholism was associated with more fatty infiltration and less liver-cell damage than other causes of cirrhosis. The presence of ascites coincided most frequently with the finding of scarring of the portal triads. The most valuable indices of liver function were found to be the cephalin–cholesterol flocculation test, thymol-turbidity test, and the plasma albumin level, in that order.

The authors emphasize that these correlations are statistical and therefore not necessarily [nor in fact] true in individual cases. *R. B. Terry*

727. **Mucolytic Enzyme Systems. X. Serum Hyaluronidase Inhibitor in Liver Disease**

G. G. Snively and D. Glick. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1087–1090, Aug., 1950. 13 refs.

Hyaluronidase inhibitor in the serum in liver disease was determined and the results were compared with those of a variety of liver function tests. Hyaluronidase action was measured by a viscosimetric method, hyaluronic acid from human umbilical cord being used. Normal serum showed a mean inhibition of 21·5%. In cirrhosis and in the various types of virus hepatitis mean inhibition was from 40 to 52%. In one case of carbon tetrachloride poisoning, an inhibition value of 94% was obtained. This inhibitory effect was destroyed by heating to 60° C.; it was therefore not due to bile constituents, which are heat-stable. There was a statistically significant correlation between rises in hyaluronidase inhibition and alkaline-phosphatase, total cholesterol, and bilirubin values and bromsulphalein retention, but there was no such correlation with the results of other tests such as total serum protein estimation, cephalin-flocculation, thymol-

turbidity, or urinary urobilinogen or cholesterol ester values. The high inhibitor level fell with clinical recovery. *C. L. Cope*

728. **Studies on the Use of Aureomycin in Hepatic Disease. III. A Note on Aureomycin Therapy in Hepatic Coma**
J. D. FARQUHAR, J. STOKES, C. M. WHITLOCK, L. W. BLUEMLE, and J. M. GAMBESICA. *American Journal of Medical Sciences* [*Amer. J. med. Sci.*] **220**, 166–172, Aug., 1950. 1 fig.

A girl aged 6 years who was suffering from chronic myelogenous leukaemia, developed acute viral hepatitis and became comatose. Thereupon aureomycin was administered intramuscularly in a dosage of 100 mg. every 6 hours for the first 7 days and by mouth in a dosage of 250 mg. every 6 hours for the next 13 days. After 24 hours' treatment the patient recovered consciousness and became mentally alert. She was given a blood transfusion, infusions of plasma and glucose, large doses of vitamin K, and a diet rich in protein and carbohydrate. Apart from a transient attack of lethargy, improvement was maintained. The jaundice subsided and the liver gradually ceased to be enlarged and tender. One month after the beginning of treatment liver function was almost normal, but there was no change in the leukaemic condition. The treatment was also successful in another young girl with acute viral hepatitis and liver failure.

Aureomycin was also given in 2 cases of portal cirrhosis. Both patients gave a history of alcoholism. The first patient, a man aged 37 years, was admitted to hospital in a state of cholaemia. He remained comatose for 3 days, then gradually recovered from the attack of liver failure, but the signs of portal cirrhosis persisted. The total dose of aureomycin amounted to 67 g. The second patient was a man, aged 60 years, with diffuse hepatic fibrosis and hepatic insufficiency. Three successive attacks of coma were relieved by intravenous injections of aureomycin. It is possible that the antibiotic exerted a direct action on the liver. Alternatively, the antibacterial action may have produced the result. *A. Garland*

729. **Studies on the Use of Aureomycin in Hepatic Disease. IV. Aureomycin Therapy in Chronic Liver Disease. With a Note on Dermal Sensitivity**
J. M. SHAFFER, L. W. BLUEMLE, V. M. SBOROV, and J. R. NEEFE. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220**, 173–182, Aug., 1950. 2 figs., 1 ref.

Aureomycin was administered by mouth to 13 patients with chronic hepatic disease. Usually the dose was 2 g. daily for 30 days. Improvement was recorded in 7 cases, but no beneficial effect was observed in 2 cases of moderate to severe portal cirrhosis and in 4 cases of chronic hepatitis after acute viral hepatitis. Some difficulty was experienced in evaluating the action of the antibiotic, for the factors requiring consideration included the effect produced by the variable intake of alcohol and the beneficial effect produced by rest in bed and by injections of albumin and glucose. Nevertheless, in the case of a young woman with diffuse hepatic fibrosis there appeared to be no doubt that aureomycin therapy had brought about a pronounced clinical improvement and a fall in the level of bilirubin in serum. A relapse occurred soon after the cessation of treatment. Another patient showed improvement both in clinical condition and in liver function.

Dermal sensitivity to aureomycin was observed in 5 cases. Exposure to sunlight seemed to cause the appearance of skin changes in 4 patients, a phenomenon which pointed to the photosensitizing effect of the antibiotic. Nail changes occurred in 3 cases. Erythema, papulo-vesicular lesions, and exfoliation developed on the hands of a patient who was exposed to sunlight on the tenth day of aureomycin therapy. Subsequently the patient's thumbnails became discoloured and were loosened from the nail bed. Gradual improvement in the condition of the nails occurred when the treatment was discontinued.

Toxic reactions to the treatment included nausea, anorexia, diarrhoea, and pruritus in the rectal region. In only one instance was the reaction severe enough to warrant the discontinuance of therapy. *A. Garland*

730. **Clinical, Biological, and Histological Study of Fatty Liver in Alcoholics; 82 Observations.** (Étude clinique, biologique et histologique des stéatoses du foie chez les alcooliques. A propos de 82 observations)
R. CACHERA, M. LAMOTTE, and S. LAMOTTE-BARRILLON. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 3497–3514, Sept. 6, 1950. 20 figs., 34 refs.

A careful analysis of 82 cases of chronic alcoholism was carried out. Liver function tests and liver biopsies were performed. In 21 cases the clinical picture was that of hepatic cirrhosis, and in 61 of " congestive hepatitis of alcoholics ".

The most relevant finding was the rarity of changes in the liver function in the non-cirrhotic cases. The most important abnormality found was an increase in the amount of total plasma protein with a reversal of the albumin–globulin ratio. All the other tests performed revealed little deviation from the normal. The cirrhotic cases showed the customary changes.

Histological examination in the non-cirrhotic cases revealed varying degrees of fatty infiltration of the liver. The nuclei of the liver cells usually remained intact, and the glycogen content of the unaffected portion of the liver seemed to be within normal limits. Some glycogen could often be found even in the cells with a high fat content. Some degree of fibrosis occurred also in the non-cirrhotic group. *R. Schneider*

731. **The Evolution of the Alcoholic Fatty Liver Studied by Puncture-biopsies.** (L'évolution des stéatoses alcooliques du foie controlée par ponctions-biopsies)
R. CACHERA, M. LAMOTTE, and S. LAMOTTE-BARRILLON. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 3515–3521, Sept. 6, 1950. 2 figs., 27 refs.

Thirty cases of fatty liver and 10 cases of frank hepatic cirrhosis were studied with the help of liver biopsies. The progress of cases of fatty liver does not seem to

follow any definite pattern. In certain cases the amount of fatty infiltration remained unaltered over a long period and was independent of changes in the degree of intemperance or of treatment. Regression and complete disappearance of the lesion occurred in others. In some cases the disappearance of the fatty infiltration was accompanied by the appearance of a frank clinical cirrhosis. Reduction in alcohol consumption and increase in protein in the diet seemed more beneficial than the administration of lipotropic factors.

The possible correlation of parenchymatous changes and mesenchymal reactions is discussed, but no definite relation could be made out. The stimulus for mesenchymal proliferation is quite unknown. The complexity of the problem is stressed. *R. Schneider*

732. **Some Physiological and Pathological Concepts in Alcoholic Fatty Liver.** (Notions physio-pathologiques sur les stéatoses alcooliques du foie)
R. CACHERA, M. LAMOTTE, and S. LAMOTTE-BARRILLON. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 3521–3527, Sept. 6, 1950. Bibliography.

The literature on the pathogenesis of fatty liver is reviewed. The authors admit the importance of the dietary factor in the genesis of fatty liver, as shown by the results of animal experiments with deficient diets and by the finding of fatty liver in some poorly nourished but strictly temperate communities. In many of their own cases, however, fatty degeneration in the liver occurred in alcoholic subjects who neither were undernourished nor took an unbalanced diet. They therefore believe that dietary deficiency is not the only reason for the development of the fatty liver in the alcoholic.
R. Schneider

See also Sections Pathology, Abstracts 552 (*a*) and (*b*); Paediatrics, Abstract 620.

PANCREAS

733. **Serum Amylase Response to Morphine, Mecholyl and Secretin as a Test of Pancreatic Function**
J. O. BURKE, K. PLUMMER, and S. BRADFORD. *Gastroenterology* [*Gastroenterology*] **15**, 699–707, Aug., 1950. 17 refs.

Working at the McGuire Veterans Administration Hospital, Richmond, Virginia, the authors compared the efficacy of the following drugs or combinations of drugs in producing an increase in serum amylase concentration: morphine sulphate, methacholine (" mecholyl ") chloride, and secretin, and methacholine, secretin, and morphine all together. In 3 patients without pancreatic disease given 16 mg. of morphine sulphate the serum amylase level rose by 55% to 232% of the pre-test value. In 2 patients given 10 mg. of methacholine and 1 unit of secretin per kg. body weight there was a rise in serum amylase level of 100% and 328% respectively, and in 6 patients given all three drugs the serum amylase level rose by 84% to 412% of the pre-test level. It was concluded that the combination of methacholine and secretin, given alone, is variable in action, and the resulting rise in serum amylase level is less significant statistically than when all three are given.

In an attempt to apply these findings in a test of pancreatic function, the following procedure was adopted: blood was taken for serum amylase determination, and 16 mg. of morphine sulphate was then given subcutaneously, followed after 30 minutes by 10 mg. of methacholine and 1 unit of secretin per kg. body weight. Blood samples were taken at intervals of 30, 60, 120, and 180 minutes. [It is not made clear whether the first blood sample was taken 30 minutes after giving the morphine or 30 minutes after the other two drugs were given.] Ten healthy subjects and 53 hospital patients, without pancreatic disease so far as could be ascertained, were tested. Of the 10 healthy subjects 4 showed no increase in serum amylase level, the mean fasting value (estimated by Bray's method) being 33·4 units per 100 ml. and the mean maximum value being 99·5 units per 100 ml. Ten of the 53 patients showed no increase in serum amylase content during the tests. The mean pre-test value for the group was 39·5 units per 100 ml., rising to a mean maximum of 82·9 units per 100 ml. after the drugs had been given. In 3 cases of achlorhydria there was a rise in serum amylase level, but in one case each of lymphadenoma, abdominal carcinoma, Whipple's disease, and lead poisoning there was no response. The mean response in 11 patients with diseases of the liver and biliary tract was statistically normal, though 7 did not respond at all. Eleven tests on 8 patients known to have diseases of the pancreas showed a significantly lower fasting amylase level (21·5 units per 100 ml.) than in the normal group. In response to the drugs, the serum amylase concentration rose to a mean maximum of 46 units, there being no increase in 5 cases. It is concluded that an apparent rise in serum amylase level of less than 50% after the administration of morphine, methacholine, and secretin is not significant. A normal response to the test does not exclude pancreatic disease, especially of the chronic relapsing type. *Walter H. H. Merivale*

734. **Incomplete Pancreatic Deficiency in Cystic Fibrosis of the Pancreas**
G. E. GIBBS, W. L. BOSTICK, and P. M. SMITH. *Journal of Pediatrics* [*J. Pediat.*] **37**, 321–325, Sept., 1950. 2 figs., 11 refs.

The complete picture of fibrocystic disease of the pancreas is gradually being unfolded. At first, naturally, the clinical effects of a 90% defect of exocrine function were most readily recognized, together with the association with pulmonary disease. The present paper adds two to the number of cases in which pancreatic involvement has been considerably less. In one the vitamin-A absorption curve was nearly normal; in the other the trypsin content of the duodenal juice was in the normal range at 8½ months, but *nil* later. Both were fatal, but probably more because of pulmonary than pancreatic degeneration. It is well known for cases of pancreatic fibrocystic disease to be found among children with bronchiectasis treated in thoracic units, and a family has recently been described in which two generations were affected. *W. G. Wyllie*

Endocrines

735. **Effect of 17-Hydroxy-11-Dehydrocorticosterone (Compound E) and of ACTH on Arthus Reaction and Antibody Formation in the Rabbit**
F. G. GERMUTH and B. OTTINGER. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74,** 815–823, Aug., 1950. 5 figs., 12 refs.

The development of the Arthus reaction in rabbits given repeated intracutaneous injections of crystalline egg albumin was suppressed by the simultaneous injection of cortisone acetate or (to a less extent) of adrenocorticotrophin (ACTH). There was a close correlation between the antibody nitrogen content of the serum and the severity of the skin reaction in both treated animals and controls, indicating that cortisone and ACTH diminish the production of antibody. Moreover, when antibody was injected intracutaneously it was found that the Arthus reaction developed equally well in treated and in untreated animals. This demonstration that these hormones inhibit the development of the Arthus reaction by suppression of antibody formation is pertinent in view of the present emphasis on the general increased resistance to stress supposedly produced by treatment with these substances. *A. C. Crooke*

736. **Experience with Protein Bound Iodine (PBI); the Effect of ACTH and Cortisone on Thyroid Function**
J. D. HARDY, C. RIEGEL, and E. P. ERISMAN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220,** 290–292, Sept., 1950. 13 refs.

737. **Cerebral Circulation and Metabolism in Hyperthyroidism**
P. SCHEINBERG. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29,** 1010–1013, Aug., 1950. 22 refs.

Cerebral circulation rate in 9 cases of hyperthyroidism was measured by the nitrous oxide method of Kety and Schmidt. Cerebral blood flow did not differ significantly from the normal. Cerebral oxygen consumption was also estimated to be normal. Arterio-venous oxygen differences were rather lower than expected; this is believed to be due to the entry of blood from the skin of the face into the internal jugular vein. The author points out that so far no effective means of increasing cerebral metabolism has been found, and suggests that this is normally close to the maximum rate. *C. L. Cope*

738. **Correlative Observations on Cerebral Metabolism and Cardiac Output in Myxedema**
P. SCHEINBERG, E. A. STEAD, E. S. BRANNON, and J. V. WARREN. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29,** 1139–1146, Sept., 1950. 2 figs., 23 refs.

Cardiac output was measured in 7 patients with myxoedema, and in another 8 similar cases the cerebral blood flow, cerebral oxygen and glucose consumption, cerebral vascular resistance, and arterial oxygen saturation were estimated. For comparison, similar observations were also made on normal subjects. It was found that all the above values were consistently reduced in cases of myxoedema with the exception of the cerebral vascular resistance, which was increased by as much as 91% over the mean normal value.

The authors suggest that mental symptoms in myxoedema are the result of decreased cerebral oxygen and glucose metabolism and that the reduction in cardiac output is " secondary to a generalized reduction in organ blood flow ". The reduction in cerebral metabolism appears to result from lack of thyroid hormone, but the mechanisms by which cerebral vascular resistance is increased, organ blood flow reduced, and cardiac output diminished remain unclarified. *S. Karani*

739. **A Correlative Study of the Cardiac Output and the Hepatic Circulation in Hyperthyroidism**
J. D. MYERS, E. S. BRANNON, and B. C. HOLLAND. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29,** 1069–1077, Aug., 1950. 28 refs.

In 14 patients with thyrotoxicosis and a mean increase in basal metabolic rate of 54%, the cardiac output was measured by direct Fick principle, and hepatic blood flow by the method of Bradley with a catheter in the hepatic vein. The percentage extraction of bromsulphalein (normal 52) was reduced to about 37. Although the cardiac output was much increased, liver blood flow was not significantly raised. Oxygen consumption in the splanchnic area was shown to be raised proportionately more than in the body as a whole. Thus the splanchnic oxygen extraction was increased, the splanchnic arterio-venous oxygen difference being raised by about 50%. It is suggested that the high uptake of oxygen by the liver, together with the normal blood flow, may account for the centrilobular necrosis sometimes seen in hyperthyroidism. *C. L. Cope*

740. **Propylthiouracil in Thyrotoxicosis; Alternate Cases Treated Medically and Surgically.**
N. TAYLOR, A. LARGE, and P. NOTH. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220,** 362–372, Oct., 1950. 5 figs., 12 refs.

During a period of 2 years, 90 patients with hyperthyroidism came under observation at the Detroit Receiving Hospital. Of 52 of these cases in which the diagnosis was considered to be adequately established uncomplicated thyrotoxicosis was present in only 9, and the disease was characterized by severe toxicity in more than two-thirds of the series of patients. For the purposes of the investigation here reported, patients with diffuse toxic goitre were assigned alternately to medical and surgical groups for treatment, but all those with toxic nodular goitre were advised to undergo thyroid-

ectomy; of the 52 cases medical treatment was employed in 25 and thyroidectomy was performed in 27. In the management of the former group propylthiouracil was administered in a dosage of 100 mg. every 8 hours, the diet being of a high caloric value, rich in proteins and vitamins. Unfortunately, 10 patients failed to attend for the final assessment of the effect of therapy, and sustained remissions were encountered in only 3 instances. The surgical patients were treated with propylthiouracil until the basal metabolic rate had become almost normal; then iodine was given for 3 weeks, and subtotal thyroidectomy was performed. It was considered on the whole that surgical intervention had produced satisfactory results, although hypothyroidism developed in 3 cases. During the 2 years after operation one patient died of carcinoma of the colon and another of gastro-intestinal haemorrhage, but there were no deaths which could be attributed to thyrotoxicosis. In cases of diffuse goitre the total dosage of propylthiouracil given before operation ranged from 29·8 to 37·8 g., and in those of nodular goitre from 77·6 to 85·6 g. Agranulocytosis occurred in one case and a pronounced increase in exophthalmos occurred in 5 cases.

The authors conclude that subtotal thyroidectomy is the treatment of choice for diffuse goitre with hyperthyroidism, and should certainly be undertaken when any tendency is seen for exophthalmos to become progressive in patients treated with propylthiouracil. On the other hand, when operation on an untreated patient involves too great a risk, prolonged administration of propylthiouracil is advisable in order to reduce the hazard and enable the surgeon to proceed with the operation.

A. Garland

741. **The Effect of Thyroid Powder on the Lethal Dose of Adrenaline.** [In English]
P. PELTOLA. *Annales Medicinae Experimentalis et Biologiae Fenniae* [*Ann. Med. exp. Biol. fenn.*] **28**, Suppl. 4, 1–59, 1950. 8 figs., bibliography.

Clinical observations suggest that thyrotoxic patients are particularly susceptible to the action of adrenaline. A similar relationship between the secretions of the two glands can be demonstrated in mice and has been made the basis of a method for assaying the potency of thyroid powders.

The LD 50 of adrenaline given subcutaneously in mice is about 7 μg. per g. body weight. This value is very constant for mice of the same strain, is unaffected by the season of the year or the sex of the mouse, but is increased when the mice are kept in a warm room (30° C.) and decreased when they are kept in the cold (10° C.) or in darkness. When thyroid powder is fed to the mice, the LD 50 of adrenaline is reduced and the amount of the reduction bears a linear relation to the dose of thyroid powder. The powder is administered by injecting a suspension of it into pieces of bread and ensuring that all this bread is eaten before any other food is given. The maximum depression of the LD 50, which occurs after 12 days of feeding, is only 1 μg. per g. when the daily dose of thyroid powder is 15 mg. per 20 g. Statistical analysis of the author's experimental results demonstrates the reliability of the method. *Peter C. Williams*

742. **Adrenocorticotropic Activity of Blood-plasma Extracts**
J. BORNSTEIN and P. TREWHELLA. *Lancet* [*Lancet*] **2**, 678–680, Dec. 2, 1950. 1 fig., 11 refs.

743. **Response to Adrenocorticotropic Hormone and Cortisone in Persons with Carcinoma, Leukaemia, and Lymphosarcoma**
T. D. SPIES, R. E. STONE, G. GARCIA LOPEZ, F. MILANES, R. LOPEZ TOCA, and A. REBOREDO. *Lancet* [*Lancet*] **2**, 241–244, Aug. 12, 1950. 4 figs., 5 refs.

Three patients with inoperable squamous-cell carcinoma, 5 with acute leukaemia, and 2 with lymphosarcoma were given either pituitary adrenocorticotrophin (ACTH) or cortisone. The patients were selected after careful histopathological investigation.

In 2 of the 3 patients with carcinoma, the tissues of the tongue, mouth, and regional lymph nodes were involved in neoplasms of large anaplastic epithelial cells of squamous type. The third tumour was a grade-II squamous-cell carcinoma of the lower lip. This last case showed considerable clinical improvement after a total dose of 270 mg. ACTH in 5 days. The other 2 patients had more severe metastatic involvement and the improvement was less. Each received 3 g. of cortisone in divided doses of 150 mg. daily by intramuscular injection. There was a striking improvement in sense of well-being and in appetite. Pain diminished, so that the amount of narcotics could be considerably reduced. Despite the large amount of cortisone administered, there was no evidence of upset of salt and water metabolism. In each of these cases the lesions decreased in size but tumour cells remained.

In the 5 patients with acute leukaemia the response varied. One died within 4 days without improvement, one improved slightly but not greatly, 2 improved a great deal, and in one the improvement was so marked that it was difficult to find a pathological cell in bone-marrow smears. One patient, under observation for a year, had two series of ACTH injections each lasting for 14 days at a dosage level of 100 mg. in 24 hours. The appetite and mental outlook of these patients improved, and from the time ACTH administration began blood transfusions were unnecessary.

In both patients with lymphosarcoma the involved lymph nodes decreased rapidly in size when cortisone was given. Fever disappeared and strength returned. They became symptom-free for a few weeks, then the symptoms returned. The patients were treated again with similar results.

In all 10 patients there was objective evidence that the disease did not disappear. The authors suggest that, even if the results are variable and unpredictable, ACTH and cortisone are promising tools in the investigation of malignant tumours. *N. R. W. Taylor*

744. **Preliminary Report on " H 365 " (*para*-Oxypropiophenone), a Synthetic Pituitary Inhibitor.** (État actuel du H–365 (para-oxypropiophénone) frénateur hypophysaire de synthèse)
M. PERRAULT. *Presse Médicale* [*Pr. méd.*] **58**, 1010–1013, Sept. 27, 1950. 17 refs.

Dermatology

745. Thorium-X Investigations: Histological Study of Thorium-X Application on Rabbit Skin
H. C. FISHMAN. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **15**, 71–74, Aug., 1950. 2 figs., 2 refs.

The hair was removed from the backs of 5 white rabbits by the application of barium sulphide. An alcoholic solution of thorium-X, 1,000 electrostatic units per ml. was applied. Biopsy specimens were taken at weekly intervals for 6 weeks. Hyperkeratosis appeared in the second week and reached its maximum one week later; it persisted throughout the period of study. In the first week vacuoles appeared in the cytoplasm of the prickle cells; they did not increase after the third week. There was occasional transient acanthosis in the first week. These changes were not seen in control sections from an untreated rabbit. *E. Lipman Cohen*

746. Basophilic Intranuclear Inclusions in Warts, Psoriasis, and Certain Malignancies
E. MEIROWSKY and L. W. FREEMAN. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **15**, 49–59, July, 1950. 5 figs., 24 refs.

The technique is described by means of which basophilic intranuclear inclusions have been demonstrated by the authors in tissue from cases of warts, psoriasis, and carcinoma.

These bodies were seen to develop in normal epithelial cells by a process of margination of chromatin or by its condensation in the centre of the nucleus, forming irregular lumps of altered chromatin which reduce osmic tetroxide and silver nitrate. This process is followed by a spreading stage, in which the entire nucleus is filled with altered chromatin, and finally the nuclear membrane is ruptured and the altered material liberated. The significance of these findings in relation to the possible virus aetiology of these diseases is discussed.
James Marshall

747. Podophyllin in the Treatment of Eczema. (Résultats du traitement de l'eczéma par le podophyllin)
X. VILANOVA, C. CARDENAL, and A. POU. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **10**, 374–384, July–Aug., 1950. 6 figs., 4 refs.

A résumé is given of the results of experimental clinical, and histological studies of the action of podophyllin in the treatment of eczema. It is stated that the drug has a remarkable drying effect on the epithelium. However, podophyllum resin, which is not constant in quality and has a local irritant action (though it is seldom a sensitizer), can be advantageously replaced by crystalline podophyllinotoxin, one of its constituents. The treatment of 116 patients with 1% podophyllum (alone or with 5% coal tar) or with 1 in 5,000 podophyllinotoxin (alone or with coal tar) caused rapid drying of lesions, decongestion, and diminution of spongiosis.
James Marshall

748. Reactions Produced by Arthropods Directly Injurious to the Skin of Man
R. M. GORDON. *British Medical Journal* [*Brit. med. J.*] **2**, 316–318, Aug. 5, 1950. 2 refs.

749. Cutaneous Sarcoidosis as an Expression of Syphilis. Report and Discussion of a Case
E. T. BERNSTEIN and M. LEIDER. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **15**, 75–79, Aug., 1950. 3 figs.

A housewife, aged 33, complained of an eruption on the arms and trunk. At the age of 15 she had contracted syphilis and had received an intensive course of antisyphilitic treatment; at the age of 20 she had had pleurisy with effusion. The eruption had started on the right arm 18 months before she was seen. It spread to the other arm and to the trunk. It was an extensive, papulonodular, erythematous, and violaceous rash with grouped lesions. Extensive pathological investigations were undertaken, the findings being as follows: Wasserman reaction, 4 plus; Kline reaction, 4 plus; radiograph of chest, normal; intracutaneous tuberculin tests: 1 in 1,000,000, 1 plus; 1 in 100,000, 1 to 2 plus; 1 in 10,000, 2 to 3 plus; B.C.G. vaccination, visible reaction in 24 to 48 hours, proceeding rapidly through all stages to scarring. Histological examination revealed the picture of sarcoid without giant cells. Penicillin, 11,300,000 units in 4 weeks, was administered. The eruption cleared rapidly and at the end of the course of treatment only very slight erythema and pigmentation remained.

This case supports the view that sarcoid is a clinical and histological entity which may occur during, or as an expression of, several infectious diseases and some non-infectious disease mechanisms. *E. Lipman Cohen*

750. Treatment of Superficial Trichophytosis with CO_2-Snow. An Attempt at Artificial Immunization ("Imitated Kerion"). [In English]
H. HAXTHAUSEN. *Acta Dermato-Venereologica* [*Acta derm.-venereol., Stockh.*] **30**, 405–416, 1950. 2 figs. 10 refs.

It has been noted that superficial patches of trichophyton infection of the smooth skin tend to clear without local treatment if kerion of the scalp or beard is also present. This spontaneous cure may be due to immunization affecting the entire skin surface. The author believes this immunity to be pronounced and of long duration, no re-infection with trichophyton fungi having been seen at the Rigshospital, Copenhagen, over a period of years in patients who have suffered from kerion, although, being mostly country dwellers, they are exposed to such infection. Kerion confers no immunity against epidermophytosis of the feet.

In the treatment of patients suffering from infection of the smooth skin with the ectothrix group of fungi, an artificial kerion was produced by one application of

carbon-dioxide snow for 5 seconds with firm pressure. After a moderate reaction with redness and infiltration the lesions cleared in a few weeks. Where multiple patches of fungus infection were present only one was treated with carbon-dioxide snow, the others clearing spontaneously, though slowly. This was thought to be due to the production of immunity, as with a true kerion infection. Two patients developed a trichophytid eruption after snow treatment.

The author suggests that the effect of iodine and chrysarobin on fungous infections may not be fungicidal but result from the inflammation provoked, as in the response to carbon-dioxide snow. *S. T. Anning*

751. **The Phagocytic Activity of Blood of Patients with Staphylococcal Skin Lesions.** (Фагоцитарная активность крови у больных стафилодермиями)
L. V. Solov'eva. Вестник Венерологии и Дерматологии [*Vestn. Vener. Derm.*] No. 4, 19–22, July–Aug., 1950.

The phagocytic activity of the blood of patients suffering from staphylococcal skin infections was investigated. The blood was examined before, during, and after a course of treatment with staphylococcal " antifagin "; a citrated sample was incubated with a staphylococcal suspension at 37° C. for 30 minutes, and smears were then made and examined. The degree of phagocytosis was estimated from the number of leucocytes which had taken up bacteria and the number of organisms contained in them. The degree of phagocytosis in 250 patients with staphylococcal skin infections did not differ essentially from that in 100 healthy control subjects. During the course of antifagin injections the degree of phagocytosis rose, reaching a maximum after 10 to 12 injections. The opsonic index rose as a result of antifagin treatment, but returned to normal levels from 5 to 30 days after the end of treatment. *D. J. Bauer*

752. **Treatment of Staphylococcal Skin Lesions with " Antifagin ".** (Опыт лечения стафилодермий антифагином)
K. L. Golshmid and B. M. Datskovskij. Вестник Венерологии и Дерматологии [*Vestn. Vener. Derm.*] No. 4, 22–25, July–Aug., 1950.

" Antifagin " treatment was tried on 3,777 patients with suppurative skin lesions of up to 6 years' duration; 2,946 patients were miners and 673 were metal workers. An average of 5 daily injections was given, together with local treatment. Complete healing after one course occurred in 1,789 out of 2,320 miners with furunculosis (77·1%); two courses produced a cure in 347, but were ineffective in 184 cases; the total success rate was 92%. Underground workers did not respond so well to treatment, presumably because the disease was aggravated by the conditions of work. Cure was also obtained in 87% of 382 miners with carbuncle and 74·1% of 244 with hidradenitis, but treatment was ineffective in 150 cases of eczema with suppurative complications. Injection of antifagin was followed by a skin reaction in 70% of cases and a general reaction in 40%. Favourable effects were also obtained in the treatment of metal workers; 92·7% of 594 patients with furunculosis were cured by one course of treatment. *D. J. Bauer*

753. **The Use of Antifagin in Pyodermitis.** (Опыт применения антифагина при пиодермитах)
A. F. Novosel'skaja. Вестник Венерологии и Дерматологии [*Vestn. Vener. Derm.*] No. 4, 25–29 July–Aug., 1950. 13 refs.

Furunculosis was treated with " antifagin " in courses of 5 to 10 daily subcutaneous injections, beginning with 0·1 ml. and increasing to 1·0 ml. by steps of 0·1 ml. The course was repeated after 15 days where necessary, and local treatment was given as well. A skin reaction was produced in most cases, and also a general reaction with pyrexia, except with one sample of antifagin prepared from non-pathogenic staphylococci. The skin reaction was studied by injecting dilutions up to 1 in 10,000 of antifagin intradermally. Patients with staphylococcal infection reacted up to a dilution of 1 in 10,000, and controls only up to 1 in 1,000. Intensity of reaction increased after antifagin treatment. In 9 cases of sycosis the reaction was negative, even after treatment. The phagocytic index and serum precipitin reaction were also investigated during the course of treatment. The index rose in those cases which responded to treatment, but the precipitin reaction gave irregular results. Of 40 cases of chronic furunculosis treated with antifagin only 6 relapsed after the first course, and only two after the second course; similar favourable results were obtained in 27 cases of other types of staphylococcal skin lesions. Nine cases of sycosis were not improved. Favourable results were obtained in 58 cases in all, out of a total of 80 patients treated. *D. J. Bauer*

754. **Dihydrostreptomycin and Potassium Iodide in the Treatment of Tuberculosis Verrucosa Cutis**
H. M. Johnson. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **15**, 61–66, July, 1950. 4 figs., 7 refs.

Details are given of 3 cases of tuberculosis verrucosa cutis which were treated with dihydrostreptomycin and potassium iodide. Rapid clinical and pathological improvement occurred after 5 to 6 weeks' treatment. The potassium iodide proved to be a valuable adjunct to streptomycin therapy. *James Marshall*

755. **The Etiology of Poral Closure. An Experimental Study of Miliaria Rubra, Bullous Impetigo and Related Diseases of the Skin. Part I: an Historical Review of the Causation of Miliaria. Part II: the Role of Staphylococcal Infection in Miliaria Rubra and Bullous Impetigo. Part III: the Pathologic Effect of Excessive Soaping on the Pores of the Skin. Part IV: the Effect of Lipoid Solvents on the Pores of the Skin. Final Discussion of Poral Closure**
J. P. O'Brien. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **15**, 95–101, 102–133, 134–140, and 141–152, Aug., 1950. Bibliography.

In this series of papers the author describes a continuation of his researches into the aetiology of miliaria rubra. He concludes that the train of events which leads to

closure of the keratin ring at the orifice of the sweat duct varies from case to case. The chief factors are staphylococcal infection, fat depletion, and oedema of the keratin and the effect of each of these factors augments that of the others.

He is prepared, as the result of ingenious experiments which are described in detail, to attribute more significance to infection than to lipoid depletion and supports this view by describing exhaustive histological investigations.

He regards miliaria as a prototype of a common cutaneous reaction. It is a clinical manifestation of " poral closure " which is a fundamental lesion in a wide range of minor and major dermatoses, such as impetigo, especially bullous impetigo, heat rashes, some occupational dermatoses, pyodermia, and the reactions to external agents as heat and cold.

He reviews the conclusions of earlier workers in the field and particularly those of Pollitzer and Unna.

John T. Ingram

756. **Dermatomyositis.** (Zur Kenntnis der Dermatomyositis)
H. SCHUERMANN. *Archiv für Dermatologie und Syphilis* [*Arch. Derm. Syph., Wien*] **190**, 284–306, 1950. 10 figs., 18 refs.

On the basis of 21 personal cases the author gives a review of dermatomyositis from the dermatologist's point of view. Initially, there is capillary dilatation in the affected skin areas with faulty mixing of the blood constituents; thus, only plasma or lymphocytes may be present or erythrocytes may predominate. The stasis leads to oedema, with a comparatively cell-free fluid, but the latter may have a high protein and fibrin content. The penetration of this exudate into and beyond the vessel wall is thought to explain much of the subsequent damage seen. The exudate penetrates between and into the collagenous fibres, laying down an amorphous mucoid substance. The initial oedema, acanthosis, and hyperpigmentation are followed by atrophy of the epithelial tissues with compensatory hyperkeratosis and pigment incontinence. If the degree of damage is slight, complete restitution is possible. If whole blood extravasates, the damage should be regarded as irreversible. The author has not seen combinations of lupus erythematosus, scleroderma, and dermatomyositis, and believes that these conditions should be carefully separated rather than grouped together.

The facies in dermatomyositis is fairly characteristic, and it alone has led to the correct diagnosis in several cases. The face appears bloated. The tip of the nose and the chin, as well as the vicinity of the mouth and eyebrows, are pale, the rest of the face appearing dusky red; thus the pallor is easily distinguished from the pallor of nephritis or the colouring in lupus erythematosus or erysipelas. The oedema of the face is only moderate, the grooves of expression being spared, whereas in lupus erythematosus the skin is tense, and the face is round and waxy in scleroderma. Though in any of these conditions immobility of the face is a feature, only dermatomyositis gives an impression of contraction of facial muscles. The appearance is either one of sleepiness with ptosis of the lids and wrinkled brows, or of alarm, depending on how the furrows on the face become set. Other points in clinical and laboratory diagnosis, especially between lupus erythematosis and dermatomyositis, are briefly mentioned. [The facial expressions are well illustrated.]

G. W. Csonka

757. **On the Relation of the Melkersson–Rosenthal Syndrome to Cheilitis Granulomatosa.** (Über Beziehungen des Melkersson-Rosenthal-Syndrome zur Cheilitis granulomatosa)
R. RICHTER and H. O. JOHNE. *Archiv für Dermatologie und Syphilis* [*Arch. Derm. Syph., Wien*] **190**, 486–492, 1950. 5 figs., 9 refs.

The Melkersson–Rosenthal syndrome is characterized by swelling of the lips, at first intermittent, but later permanent, together with facial paralysis and a fissured tongue. Miescher described a series of patients with chronic swelling of the lips without obvious cause and with a sarcoid type of histological picture, a condition which he named " cheilitis granulomatosa ". A case is described by the present authors in which a diagnosis of the Melkersson–Rosenthal syndrome could be made, but where the histological picture was that of cheilitis granulomatosa. As no histological reports of the former are available, it is possible that the conditions are in fact identical. The aetiology remains unknown.

G. W. Csonka

758. **Some Cases of the Melanosis of Riehl.** (Quelques cas de mélanose de Riehl)
—. JOULIA, —. LE COULANT, —. L'ÉPEE, and —. TEXIER. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **10**, 364–373, July–Aug., 1950. 7 figs.

The melanosis of Riehl affects the face, exposed parts of the neck, and, rarely, the hands and forearms. It begins with erythema and oedema, after which the skin thickens, becomes dry and rough, and then scales in a manner suggesting solar erythema. Pigmentation follows, and finally cicatricial atrophy.

Recently the authors have seen a number of cases which relapsed after apparent cure by vitamin and endocrine therapy, and in which erythemato-pigmentary lesions and even lesions of the buccal mucosa resembling lichen planus developed.

On biopsy the lesions were indistinguishable from those of lichen planus; the differential diagnosis, although easily made, rests entirely on the clinical signs.

James Marshall

759. **Pityriasis Versicolor Confined to the Face.** (Pityriasis versicolor de localisation faciale exclusive)
C. AGUILERA MARURI and M. BRENA ZORRILLA. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **10**, 408–409, July–Aug., 1950. 17 refs.

The authors describe a case of typical pityriasis versicolor on the face, and particularly the chin, in a child. There were no lesions elsewhere; hyperhidrosis occurred on the palms and soles, but not on the face. The suggestion is made that the rarity of the disease in children and old people may be due to an endocrine factor.

James Marshall

Venereal Diseases

760. **Anti-chancroidal Drugs Tested by the Hetero-inoculation of Bubo Fluid from the Treated Donor**
R. R. WILLCOX. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **26**, 131–135, Sept., 1950. 4 refs.

The effectiveness of drugs against experimental chancroid infection may be tested in the following ways: (1) by auto-inoculation of bubo fluid intradermally, treating the patient simultaneously, and observing whether the experimental infection is aborted; (2) by the hetero-inoculation and treatment of volunteers; (3) by the injection of bubo fluid from the treated patient into volunteers.

In this paper the author describes the results in 12 experiments carried out by a combination of methods (1) and (3) on 75 recipients with fluid from 11 treated donors. The administration to the donor of sulphathiazole, 1 g. 4 times daily, prevented infection in 8 persons inoculated 24 to 72 hours after treatment had been started. Streptomycin, given in doses of 0·5 g. twice daily for 3 days, cured the donor and prevented "takes" in 5 volunteers inoculated 24 to 72 hours after the start of treatment; in a second experiment 2·0 g. of streptomycin on the first day and 0·5 g. twice daily for 3 days thereafter protected 6 volunteers (and the donor himself) who were inoculated 24 to 72 hours after treatment had started. Aureomycin was given to a donor in doses of 250 mg. 3 times a day for 2 days and twice daily for a further day; the donor, who was inoculated at once, showed a "take", and inoculation of 3 volunteers after 24 hours' treatment produced one "take", but inoculation 48 to 120 hours after the start of treatment failed in 10 others. Chloramphenicol given by mouth in doses of 0·25 g. 3 times a day for 3 days protected the donor, who was inoculated at the start of treatment, and 5 volunteers who were inoculated after 24 or 48 hours' treatment of the donor. Neoarsphenamine, 1·2 g. in a week, failed to cure a donor or to protect 17 out of 19 persons inoculated with fluid taken 24 to 168 hours after starting treatment; when this donor was treated with 600,000 units of penicillin in oil and wax, bubo fluid taken 48 to 72 hours later failed to infect 12 persons. Procaine penicillin, 2,400,000 units, with aluminium monostearate in one dose failed to protect the donor, but protected 2 volunteers, all of whom were inoculated with fluid taken 6 days after treatment. In a second case both donor and a volunteer failed to show "takes".

From the above it seems clear that sulphathiazole and streptomycin are effective anti-chancroidal remedies, and aureomycin and chloramphenicol slightly less so; penicillin is effective when an adequate serum level is maintained, but neoarsphenamine is almost useless. Aureomycin and chloramphenicol have considerable "all-purpose" prophylactic possibilities in venereal diseases. *T. E. Osmond*

SYPHILIS

761. **Syphilis of the Lung**
I. M. LIBRACH. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **26**, 126–130, Sept., 1950. 4 figs., 33 refs.

A case of probable pulmonary syphilis in a male aged 49 is fully reported. The general condition, loss of weight, and radiological appearance suggested tuberculosis. Investigations failed to reveal tubercle bacilli in the sputum on many occasions. Serological tests for syphilis were positive in the blood and cerebrospinal fluid. After treatment with penicillin, arsenic, and bismuth the patient's general condition improved and the lung fields gradually became clearer.

The criteria for the clinical diagnosis of pulmonary syphilis are discussed, and the difficulty in differentiating lung involvement in syphilis from tuberculosis is stressed. *V. E. Lloyd*

762. **Follman's Syphilitic Balanitis.** (La balanitis sifilitica de Follmann)
A. NAVARRO-MARTIN. *Actas Dermo-sifiliográficas* [*Act. dermo-sifiliogr. Madr.*] **41**, 791–804, June, 1950. 8 refs.

Two cases of syphilitic balanitis are described in patients infected by the same woman. Both had previously suffered from non-specific balano-posthitis. Reviewing the 51 cases previously described, the author suggests that earlier or concomitant banal balanitis causes a tissue change which accounts for the slow evolution of a syphilitic infection. *James Marshall*

763. **Studies on the Relationship of Treponemal Antibody to Probable Biologic False Positive Serologic Tests for Syphilis**
C. F. MOHR, J. E. MOORE, R. A. NELSON, and J. H. HILL. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 405–409, Sept., 1950. 3 refs.

The treponemal immobilization (TPI) test of Nelson and Mayer (*J. exp. Med.*, 1949, **89**, 369) was carried out on 256 patients in order to assess its specificity for treponematoses, especially syphilis, and to see whether it would reveal the true nature of the apparently biological false-positive reactions occurring with standard serum tests for syphilis. In the case of 126 persons with treated late syphilis, 15 of whom gave negative and 111 positive reactions to the standard tests, 121 gave positive, 1 doubtful, and 4 negative reactions to the TPI test. Of 67 patients with probable late latent syphilis the TPI test was positive in 50 cases, doubtful in 1, and negative in 16. Of 63 patients with probable biological false-positive reactions to standard tests the reaction to the TPI test was positive in 6 cases, doubtful in 1, and negative

in 56. When the findings in the TPI test were compared with those based on clinical judgment a high degree of agreement was found; thus the test was positive in 96·8% of cases of proved late syphilis, in 76·3% of cases of probable latent syphilis, and negative in 88·9% of cases giving probable biological false-positive reactions.

It appears, therefore, that the TPI test is highly specific [though it cannot be expected to distinguish between the various treponematoses] and that it may prove a valuable means of distinguishing biological false-positive reactions to the standard test for syphilis from true positive reactions. It also appears probable that the immobilizing antibody persists indefinitely, at least in cases of late syphilis, even though reagin may disappear from the serum, the two not being identical.

T. E. Osmond

764. **The Cardiolipin–Lecithin Test for Syphilis**

R. P. JAYEWARDENE and T. VELAUDAPILLAI. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **26**, 136–138, Sept., 1950. 5 refs.

The authors, working in Ceylon, carried out parallel Wassermann (W.R.) [type not stated], Kahn, and cardiolipin–lecithin flocculation (C.L.) tests on sera from patients with early and treated syphilis and from non-syphilitic persons. In 357 cases of early syphilis the W.R. gave 81·8%, the Kahn test 82·6%, and the C.L. test 88·2% of positive reactions; in 1,315 cases of syphilis under treatment the respective percentages of positive results were 44·4, 52·1, and 64·8; in 1,104 non-syphilitic persons the respective percentages of positive results were 14·4, 10·4, and 14·5. From the above it is concluded that the C.L. test is the most sensitive in detecting early cases of syphilis, but is the most likely to give non-specific reactions. The reaction tends to remain positive longest in treated cases. The same test has been shown to give fewer false-positive reactions in malaria than other tests, but an equal number in leprosy and even more in infectious mononucleosis.

[The number of false-positive results with the three tests is very remarkable, unless the non-syphilitic donors included large numbers of patients suffering from diseases known to be liable to give such reactions.]

T. E. Osmond

765. **Treatment of Early Syphilis with Penicillin and Bismuth Subsalicylate; Daily Injection of 500,000 Units of Penicillin G in Sodium Chloride Solution for Twenty Consecutive Days and Ten to Twenty Doses of Bismuth Subsalicylate at the Rate of Two a Week. Second Report**

V. PARDO-CASTELLO and O. A. PARDO. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 431–435, Sept., 1950. 4 refs.

The authors believe that the maintenance of a constant blood concentration of penicillin is not necessary for the treatment of early syphilis, and that large doses of penicillin administered over a longer period will prove more effective than the more usual shorter schemes of treatment. They also believe that the addition of bismuth to any scheme of treatment enhances its therapeutic value [an opinion that is widely held both in Great Britain and on the continent of Europe]. In 91 cases of primary and secondary syphilis 20 daily injections of 500,000 units of aqueous penicillin G were given, followed by from 10 to 20 injections of bismuth subsalicylate (0·13 g.) twice weekly. Of these patients, 43 have been under observation for 10 months to 2 years, 42 for 3 to 9 months, and 6 for 2 to 3 months. At the last examination 79 were serum-negative, 11 were serum-positive with falling titres or weak positive reactions, and only one patient had relapsed serologically.

G. L. M. McElligott

766. **The Treatment of Early Syphilis with Crystalline Penicillin G in Peanut Oil and Beeswax (P.O.B.) Employing a Treatment Schedule of 300,000 Units given Twice a Week for a Period of 8 Weeks**

N. SOBEL, L. CHARGIN, C. R. REIN, and T. ROSENTHAL. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **15**, 13–23, July, 1950. 2 figs., 11 refs.

Of 160 ambulant patients with early syphilis treated by this method 113 completed the schedule without default and 70% of these were subsequently observed for 8 to 19 months. The results in primary serum-negative and serum-positive cases compared favourably with those obtained with the same total dosage in a 16-day schedule. In secondary syphilis the results were less satisfactory. Abnormalities in the cerebrospinal fluid were found more frequently with the 8-week than with the 16-day schedule.

James Marshall

767. **The Treatment of Primary and Secondary Syphilis with Four New Schedules. A Preliminary Report on 500 Cases**

L. J. ALEXANDER, A. G. SCHOCH, and W. B. MANTOOTH. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 420–424, Sept., 1950.

The authors treated four groups of patients suffering from primary and secondary syphilis, totalling 500 cases, with the following schedules: (1) Calcium penicillin in oil and beeswax (P.O.B.), 900,000 units, bismuth ethyl camphorate, 3 ml., and oxophenarsine (" mapharsen "), 0·05 to 0·06 g., given at one visit. (2) Procaine penicillin-G in oil with 2% aluminium monostearate (P.A.M.), 1,200,000 units, in one dose. (3) P.A.M., 1,200,000 units, once a week for 2 doses. (4) P.A.M., 1,200,000 units, once a week for 4 doses. In all cases the observation period was one year. Failures are classified as relapse or reinfection [though how these are distinguished is not stated].

In serum-negative cases schedule (2) appeared to be inferior to the others; in serum-positive primary syphilis schedules (1) and (4) gave the best, and schedule (2) the worst, results; and in secondary syphilis schedule (4) gave the best, and schedule (2) the worst, results. The incidence of reinfection was twice as high in primary as in secondary syphilis [which is what would be expected]. In the series of 500 cases as a whole, schedule (4) gave the best, and schedule (2) the worst, results, the percentage of failures in the four groups being 12·3, 20·2, 13·0, and 7·5 respectively. As regards serum reactions the per-

centages of patients becoming serum-negative in each of the four groups were: primary: 83·5, 84·0, 76·5, and 76·5, and secondary: 63·4, 55·9, 57·6, and 78·3 respectively; here again schedule (4) gave the best results in secondary syphilis.

It is concluded that schedule (1) is to be preferred for the rapid treatment of primary syphilis, and schedule (4) for secondary syphilis. *T. E. Osmond*

768. **The Synergistic Action of Penicillin in Combination with Arsenic and Bismuth in Early Syphilis. A Report of 198 Patients Treated with 2·4 Million Units of Sodium Penicillin Combined with Arsenic and Bismuth**

F. PLOTKE, J. RODRIQUEZ, and G. X. SCHWEMLEIN. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 425–430, Sept., 1950. 2 figs., 4 refs.

A series of 198 patients with dark-field–positive lesions of secondary syphilis were treated in 1946 with 2,400,000 units of amorphous penicillin (40,000 units 3-hourly for 7½ days) plus 0·32 g. of " chlorarsen " (8 daily injections of 0·04 g.) plus 0·6 g. of bismuth subsalicylate (three injections of 0·2 g. on the first, fourth, and eighth days of treatment). The three drugs were administered concurrently over a period of 7½ days. Although only 103 of the total number of patients were observed for more than 2 years, the authors have assumed that the defaulters would have shown the same ratio of results of treatment as those actually observed. No serious side-effects of arsenotherapy are recorded but the chlorarsen had to be omitted, or its dosage reduced, in 32·3% of cases.

Diagnostic lumbar puncture was carried out before treatment in 195 cases, in 162 (83·1%) of which the fluid was normal. In 10 of the remaining 33 the fluid became normal after treatment, in 2 it was improved at a second examination, in 2 it was unchanged, and in a further 2 there was an increase in cells and protein. The fluid was not re-examined in the other 17 cases. Failure of treatment is noted in 29 cases, including 6 probable reinfections, the cumulative failure rate for the whole group treated being statistically assessed at 15·4% at 12 to 15 months, and 20% at 24 to 27 months. This compares favourably with failure rates of 26·8 and 37·5% at the same periods in a previous series of 266 patients with secondary syphilis treated with 2,400,000 units of penicillin alone. Though the authors recognize that the improvement in their second series may be explained partly by the use of more potent preparations of penicillin they nevertheless consider that this is mainly due to a synergistic action between the three agents used.

G. L. M. McElligott

769. **Effectiveness of Penicillin in Preventing Congenital Syphilis when Administered prior to Pregnancy**

H. N. COLE, F. PLOTKE, E. W. THOMAS, and K. H. JENKINS. *Journal of Venereal Disease Information* [*J. vener. Dis. Inform.*] **31**, 201–203, Aug., 1950. 1 ref.

The outcome of pregnancy is analysed in 341 women with early syphilis (321 with primary or secondary syphilis and 20 with early latent syphilis) treated before conception with 600,000 to 9,600,000 units of aqueous penicillin. In 58 cases 320 to 360 mg. of arsenoxide was given in addition, but no patient was re-treated during the pregnancy under review. There were 325 live births and 16 foetal fatalities (abortions, miscarriages, stillbirths, and neonatal deaths)—a mortality of 49·2 per 1,000 live births. In 1944 the stillbirth rate in New York City was 80·9 per 1,000 live births. No evidence of syphilis was found at necropsy in one stillborn infant in the present series. The baby was observed for 90 days or more in 229 instances and mother and child tested serologically. The mother was serum-negative in 190 cases, serum-positive in 31; in 8 cases the status was unknown. Two infants had syphilis; one was born of a mother who had received only 1·2 mega units of penicillin before conception and who had remained sero-resistant throughout, while the mother of the other was thought to have been reinfected late in pregnancy. No particular differences in the results of treatment were noted between women who had not been pregnant when treated and those to whom treatment had been given during a previous pregnancy. It is considered that re-treatment during pregnancy is not strictly necessary for women who have previously been adequately treated for early syphilis. *R. R. Willcox*

770. **Outcome of Pregnancies of Women Treated with Aqueous Penicillin for Early Infectious Syphilis. Prevention of Prenatal Syphilis**

H. N. BUNDESEN, J. RODRIQUEZ, H. C. S. ARON, and B. F. KORMAN. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **62**, 230–236, Aug., 1950. 10 refs.

The results are reported of treating 149 pregnant women suffering from acutely infectious syphilis with aqueous penicillin. Group A (76 women) were given 2,400,000 units of amorphous penicillin over 15 days, with a total of 160,000 units during 24 hours. Group B (73 women) received 4,800,000 units of crystalline penicillin G over 7½ days, with a total of 640,000 units during 24 hours, that is, four times as much per day as those in group A. Of the 203 pregnancies investigated, of which 74 started after the conclusion of therapy, 190 terminated in live births and 13 in foetal death. In 2 of the latter cases stillbirth was due to syphilis, but the remaining 11 foetal deaths were not related to syphilis. In group A, of the total of 99 living infants, 97 were free of syphilis, but 2 infants (from the same mother) were syphilitic. In group B, all of the 78 living infants were healthy. Therefore, the second schedule of treatment with four times the dose of penicillin per day prevents congenital syphilis with more certainty than does the first schedule.

Of the 130 women who were treated for dark-field–positive lesions during pregnancy 26 completed treatment as late as one to 50 days before delivery. Although the incidence of prenatal syphilis is expected to be higher when treatment of the mother starts late in pregnancy, no case of congenital syphilis occurred among the 24 living infants; the remaining 2 pregnancies terminated in stillbirth, which was probably due to syphilis.

T. Anwyl-Davies

Genito-urinary Disorders

771. **The Treatment of Nocturnal Enuresis.** (К методике лечения при ночном недержании мочи)
V. M. Mukhin. Невропатология и Психиатрия [*Nevropat. Psikhiat.*] **19**, No. 3, 65–67, May–June, 1950.

Nocturnal enuresis in 420 soldiers could be classified into primary and secondary types. The latter was due to some organic cause, and treatment was directed towards the elimination of that cause. The primary type was thought to be due to some conditioned reflex associated with a certain dream pattern. The aim of treatment was therefore to overcome that reflex. The patients were put for 8 to 10 days on a regimen which included a reduction of fluid intake, an increased intake of salt, and the administration of general tonics, vitamins, and bromides. They were then given nightly doses of phenobarbitone for 3 weeks. This treatment was successful in a large number of cases. Follow-up study was, however, impossible in the case of many of the discharged patients. *L. Crome*

772. **Clinical Studies with ACTH and Cortisone in Renal Disease**
G. W. Thorn, J. P. Merrill, S. Smith, M. Roche, and T. F. Frawley. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 319–354, Sept., 1950. 7 figs., 46 refs.

In this comprehensive survey every possible factor in nutrition and nursing was studied, and the fullest range of clinical and laboratory investigations was carried out, in order to determine the value of cortisone and adrenocorticotrophin (ACTH) in the treatment of renal disease.

Four patients with acute glomerular nephritis were given ACTH (total amount per individual 0·18 to 1·2 g.) for periods of 5 to 13 days; nothing was found suggesting a relation between the administration of ACTH and improvement in the clinical condition; in 3 patients a temporary increase of haematuria was seen after cessation of treatment. The same lack of relation between clinical course and treatment with ACTH or cortisone is recorded in 7 children in the subacute or chronic state of glomerular nephritis. In their case the duration of treatment—in single or repeated periods—was between 6 and 28 days, with totals of 0·36 and 2·48 g. ACTH and between 1·0 and 1·4 g. cortisone. In the group of 6 patients with the nephrotic syndrome 2 were treated with cortisone (one for 3 days only with 0·8 g., the other for 8 days with 1·2 g.); this had no effect on the course of the disease. The remaining 4 received ACTH for 5 to 21 days in single or repeated courses in amounts varying between 0·4 and 2·8 g. This resulted in dramatic increase in the excretion of sodium, chloride, and water, continuing for several days after the administration of ACTH had ceased. Although the drug affected iodide and protein metabolism, there is no evidence that the course of the nephrotic process was permanently influenced.

Six patients with disseminated erythematous lupus and evidence of renal disease received ACTH (between 0·9 and 7·5 g. each, in doses of not less than 100 mg. per day); there was no noteworthy effect on the renal disease, though all other evidences of activity of the disease showed a favourable response. Three sufferers from dermatomyositis with proteinuria derived no benefit, so far as the latter condition was concerned, from the administration of either ACTH or cortisone. *L. H. Worth*

773. **Acute Glomerulo-nephritis.** [In English]
J. Vandenbroucke and M. Hendrickx. *Verhandelingen Koninklijke Vlaamse Academie voor Geneeskunde van Belgie* [*Verh. K Vlaamse Acad. Geneesk. Belg.*] **12**, 77–99, 1950. 9 figs., 30 refs.

The authors describe 105 cases of acute diffuse glomerulonephritis, observed during the first 3 months of the disease. In 67 of the cases the glomerulonephritis was preceded by an infection of the upper respiratory tract, caused mainly by haemolytic streptococci. A review is given of the literature in favour of the allergic nature of the disease.

The impairment of kidney function may vary widely. In the beginning the glomeruli, and later the tubules, function insufficiently. The authors ascribe the development of oedema to a general increase in capillary permeability. Other factors are sodium chloride retention, lowering of the serum albumin concentration, cardiac insufficiency, and an increase in antidiuretic principle. The blood pressure also varies widely too, even in the same patient, for some unknown reason. The heart is often enlarged, myocarditis being common. Acute focal glomerulonephritis is a bacterial infection of the kidney; clinically it is impossible to distinguish between this disease and diffuse glomerulonephritis. The prognosis in the latter disease is generally good; it becomes worse, however, with increasing age of the patient. The authors' experience indicates that resolution is still possible up to one year after the attack. Persistence of albuminuria does not necessarily mean that the disease will take a chronic course. Relapses are rare.

The treatment depends on the symptoms. Restriction of salt intake is recommended, with limitation of fluids only in cases with extensive oedema or encephalopathy. A low-protein diet with abundant carbohydrates is indicated in the first phase of the disease. A short review is given of the literature on results with different diets and their theoretical basis. The authors advocate use of magnesium sulphate, lumbar puncture, and venesection in acute hypertensive encephalopathy. They have not seen any improvement from decapsulation of the kidney, splanchnic infiltration, diathermy, or radiotherapy. They employed peritoneal perfusion in one case of anuria. The patient appeared to recover, but 16 days later peritonitis developed and the anuria recurred with fatal issue. *Margaretha Adams*

Disorders of the Locomotor and Osseous Systems

774. **Therapeutic Evaluation of Deoxycortone Acetate and Ascorbic Acid in Experimental Arthritis.** (Vérification sur l'arthrite expérimentale de la valeur thérapeutique de l'acétate de désoxycorticostérone (DCA) combiné à l'acide ascorbique)
L. L. COUTU and H. SELYE. *Revue Canadienne de Biologie* [*Rev. canad. Biol.*] **9**, 258–264, Aug., 1950. 6 figs., 15 refs.

In view of the favourable results reported recently by Brownlee (*Lancet*, 1950, **1**, 157) of the use of deoxycortone acetate (DOCA) and ascorbic acid in the treatment of experimental arthritis in rats induced by means of formalin injection, the present authors have repeated his work. Their observations do not bear out Brownlee's thesis. They found no evidence of any curative value in this treatment. They point out that the conclusions Brownlee draws from his work are open to doubt on general grounds, in view of the fact that he did not use a control series of animals for his experiments.

W. S. C. Copeman

775. **Vitamin E in Rheumatism and Arthritis**
M. ANT. *Rheumatism* [*Rheumatism*] **6**, 114–121, July 1950. 21 refs.

776. **A Preliminary Report of Twenty Patients Treated with △5 Pregnenolone and Remissions in Rheumatoid Arthritis following Gold Therapy**
A. COHEN, J. GOLDMAN, A. W. DUBBS, and T. J. MCBRIDE. *Journal-Lancet* [*J. Lancet*] **70**, 264–265, July, 1950. 22 refs.

The authors had available the records of a large number of patients suffering from rheumatoid arthritis who had been treated with gold salts for a few years. Recent favourable reports of the results of treatment of such cases with cortisone, adrenocorticotrophic hormone (ACTH), and pregnenolone led them to assess their results so that the efficacy of gold and steroid therapy might be compared. The group on which they report consisted of 475 patients who had received a total of 721 courses of gold therapy and were followed up for as long as 7 years. The dosage followed the lines usual in Britain, except that the total for the normal complete course was 1·24 g. Approximately half of the patients had remissions of from 1 to 7 years, and longer. Little is known so far concerning remissions after steroid therapy, beyond the fact that they are short; continuous therapy seems, in the light of present knowledge, to be necessary, and undesirable side-effects are likely to occur as the result of prolonged therapy.

The authors have given △5-pregnenolone during the last 6 months to 20 patients in doses of 0·3 to 12·0 g. Marked improvement occurred in 12 of these and some slight improvement in 3. The authors consider nevertheless that gold salts remain the most efficacious single remedy in rheumatoid arthritis; the possibility that there may be increased benefit from a combination of gold and steroid therapy is being studied. *W. S. C. Copeman*

777. **Treatment of Rheumatoid Arthritis with Progesterone and Pregnenolone**
D. H. KLING. *Annals of Western Medicine and Surgery* [*Ann. west. Med. Surg.*] **4**, 378–382, Aug., 1950. 9 refs.

The effects of progesterone therapy in 40 cases of acute rheumatoid arthritis (32 female and 8 male) and 5 cases of ankylosing spondylitis are reported. All the patients had previously had various types of treatment (including chrysotherapy in 28 cases), some with temporary benefit, but all had relapsed.

The injection of 100 mg. of progesterone daily for 7 to 30 days was followed in 20 cases by a maintenance dose of 25 to 50 mg. twice weekly. Remission or major improvement occurred in 16 of the cases of rheumatoid arthritis, but only one of the patients with ankylosing spondylitis was benefited by the treatment. It is noted, however, that of the patients previously given chrysotherapy significant improvement had occurred at first in a similar proportion of cases. Relapse occurred shortly after cessation of treatment if no maintenance dose was given, and the maintenance dose failed to prevent deterioration in some cases, so that intermittent or continuous treatment with large doses may be necessary. There were no toxic reactions among the male patients, but menstrual disorders and post-menopausal bleeding were frequent in the females, 5 of whom also had mild skin reactions.

It is suggested that as progesterone and its derivatives are readily available and have few toxic effects their administration might be combined with gold therapy and could be continued for long periods.

Kathleen M. Lawther

778. **A Study of the Interrelations of Rheumatoid Arthritis and Diabetes Mellitus**
K. A. J. JÄRVINEN. *Annals of Rheumatic Diseases* [*Ann. rheum. Dis.*] **9**, 226–230, Sept., 1950. 11 refs.

In view of reports of the use of insulin in the treatment of rheumatoid arthritis, and because adrenocortical and pituitary hormones are secreted in increased quantities in diabetes mellitus and have recently been shown to have an important effect on rheumatoid arthritis, the author studied 1,008 patients suffering from rheumatoid arthritis and 766 patients suffering from diabetes mellitus to see if it were possible to demonstrate any interrelation between the two diseases. The incidence of diabetes among the sufferers from rheumatoid arthritis was found to be $1{\cdot}3 \pm 0{\cdot}36\%$, and that of rheumatoid arthritis among the diabetics to be $1{\cdot}7 \pm 0{\cdot}47\%$. From a comparison of these figures with those of the incidence of these conditions among the general population it is

concluded that " these two diseases have no obvious tendency either to occur together, or to avoid each other ". Among the patients in the series who suffered from both diabetes and rheumatoid arthritis, the disease which developed first seemed to progress independently and unaffected by the new disease. But in one case an exacerbation of diabetes occurred with the development of rheumatoid arthritis, and in 2 patients suffering from rheumatoid arthritis this flared up when diabetes mellitus developed.

Discussing his findings, the author points out that there is considerable evidence that in diabetes mellitus there is an increased secretion of pituitary adrenocorticotrophin (ACTH) and cortisone, and that both these hormones can produce symptoms of diabetes in man. But in his series no beneficial effect on rheumatoid arthritis was found when diabetes developed as a complication, presumably because, to prove beneficial in rheumatoid arthritis, cortisone and ACTH must be given in massive doses. He suggests that massive doses of these substances cause atrophy of the suprarenals, which, according to Selye, leads to decrease in deoxycortone secretion and benefits rheumatoid arthritis thereby.

[It is somewhat surprising to read that both ACTH and cortisone may cause suprarenal atrophy. It is usually held that, although cortisone causes atrophy, ACTH stimulates the suprarenals.] *W. Tegner*

779. **Action of 21-Acetoxy-pregnenolone (" Artisone ") Compared with that of Deoxycortone Acetate (DCA) and Kendall's Compound E (Cortisone) on Experimental Arthritis.** (Action du 21-acétoxy-prégnénolone (artisone) comparée à celle de l'acétate désoxycorticostérone (DCA) et du composé E de Kendall (cortisone) sur l'arthrite expérimentale)
L. L. COUTU. *Presse Médicle* [*Pr. méd.*] **58**, 781–782, July 5, 1950. 2 figs., 5 refs.

780. **Management of Rheumatoid Arthritis with Smaller (Maintenance) Doses of Cortisone Acetate**
E. W. BOLAND and N. E. HEADLEY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 365–372, Sept. 30, 1950. 6 refs.

Since Hench *et al.* first reported the beneficial effects of cortisone in rheumatoid arthritis it has become increasingly manifest that its action is generally temporary and that relapse occurs when administration is stopped. Furthermore, adverse effects may attend its use over prolonged periods, because the hormone influences a wide variety of metabolic functions. Hence if cortisone is to become a safe therapeutic agent, methods for prolonged administration must be devised which will avoid or minimize the unfavourable reactions while preserving the effectiveness of the drug in suppressing rheumatic activity.

In this paper preliminary studies are reported which seem to show that some severe cases and most mild cases of rheumatoid arthritis may be kept under clinical control for fairly long periods with maintenance doses of cortisone, after heavy initial dosage. It has not been found necessary to give these smaller maintenance doses every day; larger doses given every other day have equally satisfactory effects. The incidence of side-effects from the hormone was decidedly less when these smaller doses were used. With average daily doses of 65 mg. or less, signs of hypercortisonism occurred in only 8·3% of patients; with the usual daily dose of 100 mg. they developed in 33% of all cases.

[This important paper should be read in full by all workers in this field of clinical medicine.] *W. S. C. Copeman*

781. **Rheumatoid Arthritis. Effects of Certain Steroids Other than Cortisone and of Some Adrenal Cortex Extracts**
H. F. POLLEY and H. L. MASON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 1474–1481, Aug. 26, 1950. 2 figs., 18 refs.

In an attempt to elicit specific structural requirements for antirheumatic activity, 12 steroids other than cortisone, and 4 adrenal cortical extracts, were administered to 11 patients with rheumatoid arthritis and comparison was made with the effects of cortisone and adrenocorticotrophin (ACTH) in the same subjects. Except for deoxycortone acetate, of which 5 mg. was given daily, the steroids were given intramuscularly in doses equalling or exceeding the known effective range of cortisone for 1 to 2 weeks. The adrenal cortex extracts used were Kendall's adrenal cortical extract given in doses of 100 ml. daily intravenously, a lipo-adrenal extract and an extract in propylene glycol given intramuscularly, and an oral preparation given in capsules equivalent in glycogenic activity to 150 mg. cortisone daily. The last 3 preparations were given for periods of 14 to 33 days.

Significant antirheumatic activity was shown by only two of the compounds used, 17-hydroxycorticosterone (Kendall's compound F) and the adrenal cortical extract given orally in the amounts mentioned above; improvement ceased immediately the compounds were withdrawn. Euphoria, comparable to that produced by cortisone, occurred only in the case of the patient receiving the oral extract. Oedema appeared only in 2 cases receiving deoxycortone acetate and adrenal cortical extract, and facial rounding only in one patient treated with 50 to 100 mg. of compound F daily for 9 days. Withdrawal effects did not occur in any case. The erythrocyte sedimentation rate (E.S.R.) returned to normal in the patients receiving the oral adrenocortical extract and the extract in propylene glycol, and in one case it fell from 85 to 24 mm. per hour after 12 days of compound F. None of the other compounds affected the E.S.R. Increased urinary excretion of 17-ketosteroids was observed with those compounds containing a 17-hydroxyl group, with the exception of 17-hydroxycorticosterone and 6-dehydrocortisone. Increased excretion of corticosteroids was produced by compound F and 3 other steroids with an α-ketol side-chain.

From their observations the authors conclude that " the antirheumatic properties of the steroid structure are dependent on the presence of a ketone group at carbon 3, either a ketone or a hydroxyl group at carbon 11, a ketone group at carbon 20, hydroxyl groups at carbons 17 and 21, and a double bond between carbon

atoms 4 and 5". These requirements are met with only in cortisone, 17-hydroxycorticosterone, and adrenal cortical extracts containing significant amounts of these two steroids. *Ellis Dresner*

782. **Cortisone Acetate and Terramycin in Polyarthritis of Rats**
W. C. KUZELL and E. A. MANKLE. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 677–681, Aug., 1950. 10 refs.

Arthritis induced in rats by the intraperitoneal injection of cultures of pleuropneumonia-like organisms did not respond to treatment with cortisone. Failure to respond to adrenocorticotrophin had been reported previously (Kuzell and Gardner, *Stanford med. Bull.*, 1950, **8**, 83), and the authors contrast their results with those obtained by Selye (*Brit. med. J.*, 1949, **2**, 1129) with the same hormones in formalin-induced arthritis in rats. The infection-induced arthritis responded to treatment with terramycin. *A. C. Crooke*

783. **Chronic Absorptive Arthritis or Opera-glass Hand: Report of Eight Cases**
W. M. SOLOMON and R. M. STECHER. *Annals of Rheumatic Diseases* [*Ann. rheum. Dis.*] **9**, 209–220, Sept., 1950. 13 figs., 10 refs.

The authors point out that although chronic absorptive arthritis of the hand, or "opera-glass hand", has been regarded as a very rare condition associated with rheumatoid arthritis, the disorder has been described in the literature over a long period under a variety of names and is neither so rare nor of such recent origin as has been assumed hitherto. They review the literature and report 8 cases of their own, in which rheumatoid arthritis was accompanied by excessive absorption of the bones of the hands and feet. The bone destruction was far more extreme than that normally found in rheumatoid arthritis, there was no tendency to ankylosis, and the fingers would extend like telescopes when pulled. In 2 cases changes suggestive of psoriasis were found in the finger-nails, but no evidence of this condition was found elsewhere. They suggest that "the condition may be considered as an unusual variant or as an extreme manifestation of rheumatoid arthritis". *W. Tegner*

784. **Experiments in Gold-testing in Gold Treatment of Polyarthritis**
T. SVANBERG. *Annals of Rheumatic Diseases* [*Ann. rheum. Dis.*] **9**, 221–225, Sept., 1950. 2 figs., 6 refs.

The author, pointing out that the toxic complications of gold therapy are the great bugbear in an otherwise valuable form of treatment for rheumatoid arthritis, suggests that there is evidence that such reactions are a form of allergy and reviews the scanty references in the literature to skin tests of sensitivity to gold. At the Norrköping Hospital, Sweden, experiments have been carried out with a view to developing such a test, intracutaneous injections of "aurothion" (gold sodium thiosulphate), and of sodium thiosulphate as a control, being given to patients before and during treatment with gold. It was not possible to establish any correlation between the occurrence of positive reactions before treatment and the development of complications when gold therapy was started. When tests were carried out during chrysotherapy, however, it was frequently found that the reaction had changed, either from positive to negative or vice versa, and in the latter case the patient often developed complications while in hospital or after discharge. In a series of 56 cases in which repeated tests were performed it was found that toxicity symptoms developed in only 5% of the patients in whom, during treatment, the intensity of the reaction had decreased, whereas they developed in 44% of those in whom the reaction did not change, and in 95% of those in whom the reaction had become more intense. The author concludes that a change in reaction to intracutaneous injection of gold appears to indicate the probability of the development of complications, but he emphasizes that his series is as yet too limited for this conclusion to be more than tentative. *W. Tegner*

785. **Ankylosing Spondylitis in Sisters**
T. N. FRASER. *Annals of Rheumatic Diseases* [*Ann. rheum. Dis.*] **9**, 231–236, Sept., 1950. 3 figs., 15 refs.

A short review of the available evidence for the familial incidence of ankylosing spondylitis is given, followed by the case records of two sisters suffering from the disease—an unlikely occurrence in view of its predominantly male incidence. In both cases the disease was fully established and in one there were rheumatoid changes in the peripheral joints. Stress is laid on the occurrence of radiological evidence of bony erosions at the sites of muscle attachment, notably in the ischial tuberosities, where pain on pressure and on sitting may be caused. This may be the origin of the sciatic pain which is so often an early symptom of the disease. *H. F. Turney*

786. **Arachnodactyly — Status Dysraphicus — Gliosis.** [In English]
C. O. WEGELIUS. *Acta Medica Scandinavica* [*Acta med. scand.*] **138**, 249–258, 1950. 1 fig., 40 refs.

Two heredo-degenerative syndromes, arachnodactyly and status dysraphicus, are reviewed and Passow's theory of a common aetiology is mentioned. The relation between status dysraphicus and other forms of gliosis, including syringomyelia, is discussed, details of 2 cases, in father and daughter, being given. The father had a sacral spina bifida, an arm span greater than his height, a high palate, dental anomalies, and a history of enuresis until the age of 15 years. In addition to this picture of status dysraphicus, there was also evidence of other forms of gliosis—a glioma in the spinal cord and multiple neurofibromatosis.

The daughter had a dysraphy of the cervical spine with scoliosis; the left side of her body was weaker than the right with differences in the tendon reflexes and in the size of the breasts; arched palate, dental anomalies, and acrocyanosis were also present. This picture of status dysraphicus was associated with epilepsy, which has been said to be related to gliosis. She also had the spider-like extremities of arachnodactyly, and a systolic heart murmur. *E. H. Johnson*

Neurology

787. **Hyperextension of the Head: a New Technique for Study of the Spinal Subarachnoid Space.** (L'iperestensione del capo: nuova technica per l'esplorazione degli spazi subaracnoidei spinali)
V. LONGO and G. M. UCCHEDDU. *Acta Neurologica* [*Acta neurol., Napoli*] **5**, 402–411, July–Aug., 1950. 5 figs., 5 refs.

In order to find out whether spinal block exists or not Queckenstedt's test is usually carried out; compression of the jugular veins is, however, rather unpleasant for the patient. The authors have found that the same end can be achieved with less discomfort in the following way: with the patient in a sitting position, lumbar puncture is carried out and the cerebrospinal-fluid pressure read; the patient's head is then slowly extended dorsally, until maximal extension is reached. In this way the same increase of intrathecal pressure is achieved as by compression of the jugular veins. *F. K. Kessel*

788. **The Osseous Lesions of Neurofibromatosis.** (Les lésions osseuses de la neurofibromatose)
J. A. LIÈVRE and H. BLOCH-MICHEL. *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **66**, 1193–1207, July 7, 1950. 8 figs., 23 refs.

The authors describe the case of a man of 41 with neurofibromatosis, who led an active life until 1947 and then developed pain in the back and lower limbs with difficulty in walking. The clinical picture was one of dwarfism, kyphoscoliosis, and general skeletal deformity, with softening of bone suggesting an osteomalacic process. Radiographs revealed general bone demineralization and symmetrical pseudofractures of the pelvis in the pubic region (Looser–Milkman type). The blood chemistry was within normal limits and intensive treatment for osteomalacia was without effect either clinically or radiologically. Five other cases are described to illustrate the association of neurofibromatosis with hyperostosis, pseudarthrosis, hypochondroplasia, and facial hemiatrophy. The authors point out that, despite confusion in the literature, the bony lesions in Albright's disease are distinct from those seen in neurofibromatosis with osseous involvement. They also stress the fact that individuals afflicted with neurofibromatosis are always of small stature. *D. Preiskel*

789. **Neurotic Tendencies in Epilepsy**
M. D. EYSENCK. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **13**, 237–240, Aug., 1950. 12 refs.

The hypothesis that epileptics have a stronger neurotic predisposition than non-epileptic persons was tested statistically in 38 epileptic subjects by means of tests said to measure neuroticism. The group included patients with grand mal, petit mal, or both, from a wide range of educational and social backgrounds. The average age of the group was 23·2 years. All patients who were defective or incapable of regular employment were excluded. The tests comprised the word connexion list (Crown), the Maudsley questionnaire (Eysenck), and the ranking Rorschach test (Eysenck). On all three tests the average score of the epileptic group was roughly one standard deviation below that of normal groups. There was no correlation between length of illness and degree of neuroticism; the author regards this finding as incompatible with the theory that neuroticism in an epileptic is a reaction to his disease. She concludes that the results support the contention that "the patient suffering from epileptic seizures tends to be emotionally unstable, immature, and neurotic". *J. B. Stanton*

790. **Electromyography in Diagnosis of Nerve Root Compression Syndrome**
P. A. SHEA, W. W. WOODS, and D. H. WERDEN. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **64**, 93–104, July, 1950. 7 figs., 15 refs.

The purpose of this study was to determine whether lesions compressing a single spinal nerve root could be located exactly by electromyography with a cathode-ray oscilloscope and a needle electrode inserted directly into the muscle fibres to be tested. This examination was carried out in 75 consecutive cases of compression lesions of spinal nerve roots. In only 7 cases was the locality indicated by electromyography not confirmed by subsequent operation. The possible reasons for these few failures are discussed. In 68 of these cases myelography was also carried out, the level being incorrectly indicated in 10 instances. *F. K. Taylor*

ELECTROENCEPHALOGRAPHY

791. **Electroencephalographic Signs of Cerebral Tumour.** (Signes électroencéphalographiques des néoformations des hémispheres)
P. RUECH, H. FISCHGOLD, G. C. LAIRY-BOUNES, and C. DREYFUS-BRISAC. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 2612–2622, July 22, 1950. 15 figs., 13 refs.

The authors describe their routine of investigating suspected cases of cerebral tumour, and discuss those features of the electroencephalogram which they consider of localizing value: (1) polymorphic delta rhythm in a limited area; (2) local increase in amplitude of a delta rhythm; (3) local flattening of a delta rhythm; (4) local freedom of a delta rhythm from superimposed rhythms; (5) crossed phase-reversal of a delta rhythm; (6) unilateral abolition of "blocking" of alpha or mixed rhythms, indicating an occipital-lobe lesion; (7) monorhythmic *rhythmes à distance*.

The electroencephalogram is discussed in relation to the physical signs, and the authors emphasize the need, where there is disagreement, for weighing the relative values of the physical and electrical signs.

W. A. Cobb

792. **Pathological Rhythms Detected at a Distance from Cerebral Tumours.** (Rhythmes pathologiques détectés à distance des hémisphères cérébraux)
C. DREYFUS-BRISAC, G. C. LAIRY-BOUNES, S. SCARPALEZOS, and H. FISCHGOLD. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 2623–2628, July 22, 1950. 8 figs.

Certain rhythms in the electroencephalograms of some patients with cerebral tumours appear at a distance, and are distinct from the irregular (polyrhythmic) delta waves found around the tumour itself. Such "*rhythmes à distance*" were recognized in 21 out of 101 cases of hemisphere tumours, being bilaterally synchronous in 13 and present on the side of the lesion in 8; their site is anterior, usually frontal. Three types are described: (1) sinusoidal bursts of 2- to 3-cycle-per-second waves; (2) continuous "hypersynchronous" rhythm, irregular and polyrhythmic; (3) theta rhythm at 4 to 6 cycles per second, constant in amplitude. The tumours giving rise to these rhythms are, for the most part, posterior and large, and they usually invade deep structures.

W. A. Cobb

793. **A Radiological Check on Electroencephalographic Location.** (Contrôle radiologique des localisations faites en électro-encéphalographie)
H. FISCHGOLD. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 2629–2630, July 22, 1950. 2 figs.

The projection of a cerebral tumour on the scalp, as estimated electroencephalographically, is outlined by a metal thread, and lateral and antero-posterior radiographs are taken. At operation metal clips are left around the lesion, or its site if it has been removed, and similar radiographs are obtained. If, when the two lateral or frontal films are superimposed, the clips lie within the circle of metal thread the location is considered to have been good.

W. A. Cobb

794. **Some Sources of Error in Location of Cerebral Tumours.** (Quelques causes d'erreur dans la localisation des tumeurs des hémisphères)
H. FISCHGOLD. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 2631–2633, July 22, 1950. 2 figs.

During one year 57 patients with tumours of the cerebral hemispheres were examined electroencephalographically. In 24 location was good, in 6 approximate; in 11 cases lateralization only was possible, in 13 the electroencephalogram was normal or diffusely abnormal, and in 3 cases location was incorrect. The author's aim is to engender such confidence in the electroencephalogram as to make ventriculography unnecessary in those cases in which the tumour has been definitely located. He discusses the 3 cases of incorrect location and lays down certain rules of procedure in examining patients with hemisphere tumours.

W. A. Cobb

795. **Sleep as an Activator in Electroencephalography in Epilepsy of Childhood.** (Le sommeil comme activateur de l'E.E.G. dans l'epilepsie de l'enfant)
H. FISCHGOLD, G. CAPDEVIELLE, and S. SCARPALEZOS. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 2638–2641, July, 1950. 7 figs., 3 refs.

Recording of the electroencephalogram (EEG) of the child is often difficult or wellnigh impossible, but if the natural sleep pattern is studied it may be possible to select a time when the child will sleep spontaneously during the record. Failing this, sleep may be induced with a hypnotic. The technique is particularly valuable in the examination of epileptics, and contrasts with activation by convulsant drugs, in that the latter will give rise to EEG abnormalities in all subjects if in sufficient dosage.

Of 21 subjects between 6 months and 10 years of age, 14 had normal waking records. During sleep 9 of the records showed "epileptic" outbursts (spikes or spikes and waves), while only 2 of the records remained definitely normal.

[The above articles, and some others in the same issue, epitomize the work of Fischgold and his colleagues in the Neuro-psycho-surgical Centre of Ste. Anne, Paris. They form a valuable contribution in this field, not so much for any new observations which they may contain, but for the restrained yet optimistic point of view which they display.] *W. A. Cobb*

796. **Remarks on Electroencephalography in Cerebral Abscess.** [In English]
O. FARBROT. *Acta Psychiatrica et Neurologica* [*Acta psychiat., Kbh.*] **25**, 167–208, 1950. 3 figs., 20 refs.

This is a clinical and electroencephalographic (EEG) study of 7 cases of proven or suspected cerebral abscess. In each of 3 cases in which the abscess was found at operation at the predicted site there was good correlation between the clinical, EEG, and angiographic findings. The first 2 of these patients were left with considerable residual disability, despite treatment, and their EEG, recorded at intervals over periods ranging up to 8 months, showed little or no improvement. The third patient subsequently had a left-sided convulsive attack and this could be correlated with a demonstrable epileptic focus in the right frontal region. The fourth patient was admitted seriously ill, his EEG showing a severe dysrhythmia with a focus in the left parieto-frontal region. Death occurred shortly afterwards and at necropsy a large abscess was found in the left parietal region. In the remaining 3 cases the clinical findings strongly suggested the presence of a cerebral abscess. None of these patients, however, was subjected to operation, all 3 responding to penicillin therapy, although one died of meningitis 8 months later. In each of these cases there was again good correlation between the clinical and EEG findings, and during the period of clinical recovery the EEG also showed steady improvement. In all cases clear-cut focal abnormalities were demonstrable with the aid of a three-channel Kaiser instrument, monopolar and bipolar methods of recording being used. A number of records are reproduced.

In his commentary the author states his belief that in cases of acute cerebral abscess the severity of the EEG abnormality may give information about the nature of the lesion, the rate of its expansion determining the degree of dysrhythmia. He concludes that the EEG is of great value in the location of cerebral abscess, and that serial recordings are important in the evaluation of progress and also provide pointers with regard to the development of late complications. *Maurice Parsonage*

797. **The Electroencephalogram in Sleeping Children.** (L'électroencéphalogramme du sommeil chez l'enfant)
I. NEKHOROCHEFF. *Revue Neurologique* [*Rev. neurol.*] **82**, 487–495, June, 1950. 11 figs., 12 refs.

The electroencephalogram (EEG) was recorded during sleep in 30 clinically normal children between the ages of 2 months and 9 years whose waking EEG was considered normal. The examinations were made at times when it was usual for the child to go to sleep [and apparently without the aid of sedatives, such as have been used in a number of similar studies].

In older children there was first a disappearance of alpha rhythm, followed by increasing theta and delta activity; in younger children [in whom there is normally no alpha rhythm] the *rhythme de base* was first increased; there was no essential difference between the two. Later there were " spindles " of fast rhythm, rarely as fast as in the adult (14 cycles per second), and large bursts of mixed delta waves, sharp waves, and fast spindles, which the author likens to the " K complexes " well known in the adult EEG. *W. A. Cobb*

BRAIN

798. **Post-infectious Encephalomyelitis and Multiple Sclerosis. The Significance of Perivenous Encephalomyelitis**
L. VAN BOGAERT. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath. exp. Neurol.*] **9**, 219–285, July, 1950. 22 figs., 24 refs.

The author, who reported 19 cases of acute disseminated encephalomyelitis between 1927 and 1932 (the disease has now become rare), has followed up his patients, 11 of whom are alive and free of any neurological disease. Of the others, 4 have developed classical multiple sclerosis, one a condition like multiple sclerosis, while another, incompletely studied, had residua of myelitis with small perivascular foci. Of the remaining 2, one died in the acute stage of the disease and the other was untreated.

It is presumptuous, he holds, to regard perivenous encephalitis as an acute form of multiple sclerosis even if, as many maintain, there are transitional forms. Perivenous encephalitis is only one of the final histopathological pictures resulting from involvement of the central nervous system in non-specific infections, lymphocytic meningo-encephalitis and cerebral purpura being two other types. Apparently identical prodromal infections may produce any one of these results.

Two fatal cases which occurred in the year 1934 are reported; they both followed non-specific infections and presented the histopathological features of perivenous encephalomyelitis. One of these cases was of particular interest because the subject, a girl, had had diphtheria at the age of 6 followed by polyneuritis, and 2 months later measles in association with diplopia, paresis of the right internal rectus muscle, bilateral ataxia, pyramidal tract involvement, choreic movements of the right arms, and a cerebrospinal fluid containing 6 cells and 55 mg. of protein per 100 ml. She recovered completely, but developed acute disseminated encephalomyelitis at the age of 9, death occurring on the 14th day of the disease. Animal inoculation experiments were unsuccessful and no trace of old scars could be found in the brain. In this case, therefore, the transition could be observed from an attack induced by measles to one which was apparently spontaneous; the diphtheria had apparently sensitized the nervous system.

Other examples are given from the author's experience and from the literature upholding the view that perivenous encephalomyelitis gets its special character from the nature of the " terrain " rather than from the causative agent itself. Very often it would seem that " a second conflict occurs in the territories where the ground was weakened by the first battle ". *W. H. McMenemey*

799. **Epilepsy in Cases of Temporal Tumour.** (L'épilepsie des tumeurs temporales)
J. E. PAILLAS, H. GASTAUT, and J. TAMALET. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 2380–2387, July 2, 1950. 5 figs., 36 refs.

A report is given of 72 brain tumours involving the temporal lobe, the diagnosis in 69 being verified at operation and in 3 at necropsy. A detailed analysis of all manifestations of epilepsy or epileptic equivalents, is presented under 6 heads.

(1) Generalized epilepsy (grand mal) was seen in 16 cases. (2) Psycho-sensory crises were brief and might occur 20 to 30 times in the day. Twelve patients had olfactory hallucinations; 10 had auditory ones, usually non-specific noises like tinnitus, but occasionally highly organized. Two patients had hallucinations of people speaking, and one had " auditory illusions ". Fourteen had visual hallucinations. Vestibular hallucinations or vertiginous crises were observed only in 2 cases. (3) Paroxysmal alterations in consciousness. Jackson's " dreamy state " was often seen either alone or as a prelude to grand mal, and is considered to be pathognomonic of a temporal-lobe lesion. Other types in this category are considered with reference to Kinnier Wilson's classification. Characteristic *déjà vu* did not occur (but there was one case of *déjà entendu*). Wilson's " panoramic memory " was not observed. A sensation of strangeness was the most frequent of the sub-varieties seen. Lastly, Wilson's " abortive type " (similar to the " forced thinking " of Penfield) was seen occasionally. (4) Psychomotor automatisms and periods of absent-mindedness. These " absences " the authors endeavour to distinguish from those of petit mal. The commonest automatisms were the " tasting movements " of Hughlings Jackson. (5) Attacks of dysphasia. Associated with tumours of the dominant hemisphere, these were always of the amnesic type, or rather of " failure of access

to vocabulary". The brief attacks can hardly be distinguished from the "absences" of (4) above, or of petit mal. [If detected by a failure to name test objects this condition is often called "normal" aphasia, but this term is far less descriptive of the speech defect.] (6) Attacks with spread to neighbouring cortex. In 13 cases there were focal motor signs; in 3, conjugate deviation of head and eyes; in 6 paraesthesia from involvement of post-central cortex.

A short section on diagnosis is included. The epileptic phenomena are considered to be almost diagnostic of tumour. The typical electroencephalographic findings are outbursts of irregular delta waves; in the marginal regions of involved cortex theta waves appear and may enable the clinician to delimit the tumour. Ventriculography was also used in doubtful cases.

[Conventional diagrams associating the manifestations described with regional areas of the temporal lobe are included, but without support from the clinical data presented. The interesting speculation on the relation of these epileptic equivalents to the dominant autonomic nervous system representation of the medial temporal cortex is not mentioned by the authors.]

Donald McDonald

800. **Primary Mesenchymal Tumors of the Brain, So-called Reticulum Cell Sarcoma. Report of Five Cases**
C. E. TROLAND, P. F. SAHYOUN, and F. B. MANDEVILLE. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath. exp. Neurol.*] **9**, 322–334, July, 1950. 9 figs., 22 refs.

The authors object to the term reticulum-cell sarcoma on the grounds that the reticulum appears rather to be related to the blood vessels than to form an integral part of the tumour. Thus one photomicrograph reproduced shows distended rings of reticulum fibrils about to rupture around blood vessels. They prefer to call these tumours primary mesenchymal tumours, classifying them according to Broders's grading, in the way recently adopted by Kernohan *et al.* for astrocytomata, ependymomata, and oligodendrogliomata. According to this scheme, what is commonly called giant follicular lymphoma becomes Grade 1. Grade 2 embraces some of the reticulum-cell sarcomata, the remainder being in Grade 3 in company with Hodgkin's sarcoma. The clasmatocytoma, or stem-cell sarcoma, constitutes Grade 4. Five case reports form the basis of this study.

W. H. McMenemey

801. **The Clinical Picture of Tumours of the Third Ventricle.** (К клинике опухолей третьего желудочка)
R. Y. GOLANT. Невропатология и Психиатрия [*Nevropat. Psikhiat.*] **19**, No. 3, 13–19, May–June, 1950.

The psychopathological picture in 6 cases of tumour of the third ventricle consisted of a varying and alternating combination of features resembling the Korsakoff state, such as confabulation, loss of memory for recent events, and pseudoreminiscences with episodes of delirium. The general psychological background was one of somnolence and apathy with an occasional euphoria and *Witzelsucht*.

L. Crome

802. **A Clinical Study of Kernicterus.** (Estudio clinico de la ictericia nuclear)
J. M. SEGARRA-OBIOL. *Revista Española de Oto-Neuro-Oftalmología y Neurocirugía* [*Rev. esp. Oto-neuro-oftal.*] **9**, 217–243, July–Aug., 1950. 15 figs., bibliography.

After a short historical review recalling the earlier histological studies on kernicterus and Schmorl's classic description of the distribution of the biliary staining in the central nervous system, the author discusses the main clinical features of 20 cases in which the diagnosis was proved at necropsy. Since kernicterus is not a disease in itself, but a syndrome found in some of the forms of haemolytic disease of the newborn, especially icterus gravis, the same familial incidence is preserved, the first child usually being spared, after which the incidence (but not necessarily the severity) rises to a peak at the third pregnancy. In the clinical records of the National Blood Transfusion Centre in Paris from 1946 to 1948 the author found 307 cases of icterus gravis, of which 27 (9·4%) were diagnosed as having kernicterus. He regards this figure as too low, and quotes figures of up to 50% given by other authors.

Four clinical types are distinguished: (1) hyperacute; (2) acute; (3) undulant; and (4) subacute or incipient. The typical picture of the acute type is of sudden development of jaundice, most frequently during the first hour, in an apparently normal newborn child. This may remain the only sign for 24 to 48 hours, and may even be absent. Neurological signs appear most frequently on the third day, consisting primarily of somnolence passing into decerebrate rigidity. Papillitis, nystagmus, muscular spasms, athetoid movements, and tremors may occur, and the reflexes are all reduced or absent. Of the cranial nerves, the seventh, eighth, ninth, and tenth may be involved, and the thermoregulatory and respiratory centres are frequently disturbed (as in 13 cases in the author's series). In 5 cases there were pulmonary symptoms, and other visceral disturbances in the series of cases reported included hepato-splenomegaly, oedema of the legs, anorexia, diarrhoea, and haemorrhages. The haematological picture differs little from that of icterus gravis, but the anaemia is usually only moderate, erythroblastosis may be absent, and the degree of kernicterus bears no relation to the degree of iso-immunization. In the hyperacute type the infant is born already jaundiced and apnoeic and dies within 24 hours. In the acute type described above, dehydration, respiratory disturbances, hypotonia, and collapse lead to death usually within 7 days, although with exsanguination–transfusion some infants may recover permanently or temporarily. In type (3) an illusory improvement may precede ultimate deterioration or death. The subacute type may only reveal itself at a later age by the appearance of neurological sequelae such as mild hypertonia or ataxia.

The neurological signs seen in the acute stage may continue, more or less modified, in patients who survive or they may disappear, either permanently or to reappear as the central nervous system matures. The commonest syndromes are: (1) extrapyramidal, with crises of decerebrate rigidity, choreiform movements, tremors, and, rarely, hypotonia; (2) lack of motor development, with pyramidal signs; and (3) mental retardation. Less

commonly there may appear a cerebellar syndrome, epilepsy, deaf-mutism, oculomotor palsies and oculogyric crises, and disturbances of swallowing and articulation.

The author found that there was no correlation between the degree of jaundice and the severity of the kernicterus, and no feature of the jaundice was of any use as a prognostic guide. *J. B. Stanton*

SPINAL CORD

803. **The Familial Occurrence of Multiple Sclerosis and its Implications**

R. P. MACKAY. *Annals of Internal Medicine* [*Ann. intern. Med.*] **33**, 298–320, Aug., 1950. 2 figs., bibliography.

The family incidence of disseminated sclerosis has long been a matter of controversy. English and American authors make little of it, but continental medical literature contains numerous references. Out of 260 patients with disseminated sclerosis seen by the author in 20 years in private practice, 5 were patients with very near relatives similarly affected. The author believes that this occurrence is more common than could be accounted for by mere chance, and he discusses the possibility of a genetic strain of which disseminated sclerosis is the outward manifestation. The weakness of the whole theme is, of course, that the great majority of patients suffering from disseminated sclerosis do not have afflicted relatives; in many cases interrogation of the latter will reveal psychiatric or neurological taints if sufficient care is taken in the search. A number of cases are recorded of disseminated sclerosis in one member of a pair of monovular twins, and this takes a great deal of explaining. The most that can be said is that in some families there may be some inherent constitutional weakness rendering the patient liable or vulnerable to disseminated sclerosis. *G. F. Walker*

804. **Relation of Brucellosis and Multiple Sclerosis**

C. G. SPICKNALL, L. T. KURLAND, B. N. CARLE, and L. L. TERRY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 1470–1473, Aug. 26, 1950. 8 refs.

Kyger and Haden (*Amer. J. med. Sci.*, 1948, **216**, 689) first suggested that disseminated sclerosis may be due to brucellosis, their thesis being based on the finding of 115 cases of positive reaction to brucella antigen amongst a group of 118 cases of disseminated sclerosis. Twenty cases of disseminated sclerosis were studied by the present authors. Routine studies of urine and blood, serological tests for syphilis, blood culture for brucella organisms, slide and tube agglutination, and brucella skin-sensitivity tests were performed. The minimum requirement for a positive skin reaction was the production of a zone of oedema of at least 0·5 cm. diameter in 48 hours. Control skin tests were made with histoplasmin, tuberculin, and coccidioidin.

No positive blood cultures for brucellosis were found on examination of 112 specimens from the patients; guinea-pigs were inoculated with spinal fluid from 19 of the patients, also with negative results. Culture of spinal fluid was also negative. Only one patient had a positive skin reaction to brucellergin; 3 had positive reactions to a suspension of killed brucella cells. Of control skin reactions, 1 was positive to coccidioidin, 5 to histoplasmin, and 12 to tuberculin. Five out of 20 control patients gave positive skin reactions with brucella antigen.

In one case of disseminated sclerosis the agglutination titre was 1 in 20 and in another 1 in 640, the other reactions being completely negative. The first patient had had a chronic poorly-defined illness and had previously had a positive agglutination reaction to a titre of 1 in 2,560. It is concluded that he probably had had brucellosis.

The authors point out that the only certain way of establishing the diagnosis of brucellosis is by isolation of the organism from the blood and tissues. They suggest the possible occurrence of occasional neurological complications in brucellosis; this must be borne in mind when considering the possible relation between this disease and disseminated sclerosis. Though brucellosis is much commoner in rural areas, disseminated sclerosis is at least as common, if not more so, in urban communities. The evidence is opposed to any possible causal relation between brucellosis and disseminated sclerosis. *M. H. Pappworth*

805. **Brucellosis and Multiple Sclerosis**

C. W. EISELE, N. B. MCCULLOUGH, and G. A. BEAL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 1473–1474, Aug. 26, 1950. 3 refs.

These authors from Chicago investigated 52 cases of disseminated sclerosis (34 in males of an average age of 36·9). The duration of the disease varied from 3 weeks to 30 years, with an average of 7 years. A control series was formed of 104 healthy males from a penal institution. No patients in either series had had brucellosis, or any illness that was at all suggestive of this. None had been a butcher, dairyman, or meat packer. None lived in a rural area or had been inoculated with cholera vaccine. So far as is possible brucella infection was therefore excluded in all cases reviewed.

Agglutination tests, opsonocytophagic tests, and brucellergen skin tests were performed on all cases and controls. The technical details of these tests are fully described. Oedema and induration of at least 0·5 cm. diameter in 48 hours was the minimal skin response regarded as positive. Of those with disseminated sclerosis 45 gave a negative response to all three tests; 74 in the control series also gave a negative response. Only 2 patients with disseminated sclerosis had a positive skin reaction, whereas 18 of the controls gave positive reactions. Agglutination reactions were positive (but only to very low titres) in 3 of the cases of disseminated sclerosis and in 1 of the controls. There was some opsonin activity in 5 of the cases of disseminated sclerosis and in 13 controls. On the basis of these results, the authors conclude that there is no causal relation between brucellosis and disseminated sclerosis.

M. H. Pappworth

Psychiatry

806. **Neuropathological Findings in Phenylpyruvic Oligophrenia (Phenylketonuria)**
E. C. ALVORD, L. D. STEVENSON, F. S. VOGEL, and R. L. ENGLE. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath. exp. Neurol.*] **9**, 298–310, July, 1950. 6 figs., 21 refs.

Histological study of 5 cases of phenylpyruvic oligophrenia revealed a defect in myelinization in 3, and increase of fat about blood vessels and gliosis in all. The fact that myelinization was more complete in the 3 adult cases suggests that this process is considerably retarded but not completely absent in phenylpyruvic oligophrenia. The increase in fat about blood vessels and the gliosis are more likely to be related to the metabolic defect and imperfect myelinization than to be concomitant developmental defects. The same factors were responsible for the decrease in the number of Purkinje cells in the 2 cases in infancy.

As it is the current view that there is a recessive inheritance of a defect related to the enzyme controlling the *para*-hydroxylation of phenylalanine to form tyrosine, the marked retardation in myelinization noted in the 2 cases in infancy suggests that the mental deficiency may be the result of an enzymatic defect with subsequent failure of protein metabolism. *W. H. McMenemey*

807. **Disturbances in Time Discrimination in Organic Brain Disease**
J. J. COHEEN. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **112**, 121–129, Aug., 1950. 9 refs.

Awareness of the passage of time may be greatly disturbed in physical or mental disease. The author describes the use of a simple quantitative test, which may be of value in measuring cerebral impairment. "The subject is presented with a pencil and a sheet of mimeographied words of little or no subjective interest. At a given signal, he is instructed to begin encircling all the letters 'T' which he can find on the printed sheet. He is first informed, however, that at certain intervals, he will be asked how much time he feels has elapsed and in each case he must estimate the passage of time that has passed since the beginning of the test. The time intervals used are 1, 2, 4, 5, 7, and 10 minutes." In 47 out of 50 normal controls the estimates at 4, 5, 7, and 10 minutes fell within 100% deviation. In 69 patients with organic brain disease (syphilis, post-traumatic states, and so on) certain gross deviations were found.

(1) Twenty-two patients gave normal records; these were well-preserved individuals who had made good recoveries from transient confusional states on admission. (2) Nine grossly underestimated the passage of time (for example, estimating 10 minutes as 3 minutes or as 18 seconds). As a group they seemed to be characterized by being excessively emotional with impaired judgment. (3) Nineteen grossly overestimated the passage of time (for example, 10 minutes was estimated as 30 or 40 minutes). These patients showed more marked deterioration than those in group 1, with greater memory defects, and the test results roughly correlated with the degree of deterioration. (4) Nineteen patients showed loss of continuity. Thus a patient at 1, 2, 4, 5, 7, and 10 minutes from the start of the test would estimate the time lapse as 5, 5, 11, 15, 14, and 12 minutes. These patients showed still more profound deterioration, and were confused, easily fatigued, and perseverative. (5) Ten patients recovering from affective psychoses, tested an hour after an electrically induced convulsion, showed gross disturbance of temporal judgment with return to normal in 2 or 3 weeks. One patient with schizophrenia had normal responses before and abnormal 2 months after a lobotomy which had caused little clinical change. Re-testing of individual patients revealed marked consistency in the kind of response.

The author adds some theoretical comments. "The structure of temporal organization, involving as it does memory, attention, reasoning, awareness and association, is not localizable to some one portion of the brain, but is inextricably interwoven with the entire psychic organization, and is therefore vulnerable to the same deleterious and noxious influences. Thus, the interruption in proper psychic functioning is reflected in the degree of alteration or distortion of the time structure. The efficiency of the time apparatus, therefore, becomes an index of the existing efficiency or health of the psychic structure."
Elliott Emanuel

808. **A Study of the Potassium and Sodium Content of the Blood Serum in Schizophrenic Subjects.** [In English]
E. HØYRUP. *Acta Psychiatrica et Neurologica* [*Acta psychiat., Kbh.*] **25**, 179–208, 1950. 20 refs.

The author discusses the adrenal cortical hormones with special reference to the action of cortin, and reviews relevant biochemical investigations in schizophrenia. Because of the paucity of reports on sodium and potassium metabolism in this condition the investigation described was undertaken.

Serum sodium levels were determined gravimetrically after acid digestion and precipitation with zinc uranyl acetate. Serum potassium determinations were made, after acid digestion, by precipitation with platinic chloride, displacement by this of iodine from potassium iodide, and titration with N/100 sodium thiosulphate. Estimations were carried out on 14 normal controls (nursing staff) and 13 patients with acute and 13 with chronic schizophrenia at the Mental Hospital at Vordingborg, Denmark. Physical disease was excluded in all cases. The mean values for the serum sodium content were: in normal controls, 337·9 mg. per 100 ml.; in acute schizophrenia, 335·0 mg. per 100 ml.; and in chronic schizophrenia 332·3 mg. per 100 ml. The corresponding values for potassium were 18·8, 19·7, and 18·6 mg. per 100 ml.

The author suggests that the slightly lower mean serum sodium values in the two schizophrenic groups are evidence that the adrenals are concerned in the pathogenesis of schizophrenia. *J. Walker*

809. **The Immunological Properties of Alcohol. A Survey of the Literature**
M. W. ROBINSON. *Annals of Allergy* [*Ann. Allergy*] **8**, 468–487, July–Aug., 1950. Bibliography.

PSYCHOSOMATIC MEDICINE

810. **Pathogenesis of Urticaria. Experimental Study of Life Situations, Emotions and Cutaneous Vascular Reactions**
D. T. GRAHAM and S. WOLF. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 1396–1402, Aug. 19, 1950. 4 figs., 15 refs.

A group of 30 cases of chronic urticaria were investigated along three lines: episodes in the patient's personal history were correlated with the appearance of attacks of urticaria; material thought to be provocative was introduced into interviews and the skin changes were measured; the response to vasodilating agents of the patients was compared with that of a control group. The group of patients contained 17 women and 13 men. Skin temperature, as measured with a Hardy radiometer, and the reactive hyperaemia threshold (Di Palma) were employed as indices of cutaneous vascular function. Sensitivity of the skin to histamine and pilocarpine introduced by iontophoresis was determined in 24 patients and 24 controls.

In 29 of the 30 patients an almost constant relation was found between a specific attitude and urticarial attacks. In brief, the patients considered themselves wronged or injured, usually by someone in a fairly close family relationship, but could neither retaliate nor run away. In this setting, they became intensely resentful, and an attack occurred. The attitude was as a rule quite conscious and clearly verbalized. So long as the basic conflict with a loved person was unresolved, minor disturbances were often enough to provoke attacks. Some attacks were observed in which the theme situation described above did not seem to obtain. The experience of anxiety, hostility, grief, or dejection was not observed to be a precipitant of attacks. No significant association of attacks with a particular food or other allergen was noted.

All the patients were seen to flush when topics of personal concern were brought up for discussion. Five patients had urticarial attacks while discussing their problems. When resentment was aroused by a discussion of events which in the past had been associated with attacks of urticaria, capillary tone, as measured by the reactive hyperaemia test, was lower than during control periods. In 13 patients the forearm skin temperature was measured at interview; in all those who became resentful the temperature rose at the same time that minute vessel tone was decreased. Anxiety and dejection, however, were associated with increase in tone of minute vessels and with arteriolar constriction.

Of 24 patients tested by iontophoresis, 23 responded with some whealing to histamine, as against 6 controls, and 23 showed whealing with pilocarpine, as against 3 controls. In 4 patients who continued to attend the clinic after becoming free from urticaria, these responses could no longer be elicited. Ten of the 30 patients had, at one time or another, a diastolic blood pressure of 100 mm. Hg or more.

The authors conclude from this study that urticarial wheals may be regarded as the end-result of intense dilatation of arterioles and capillary vessels, with increased permeability as a consequence of this. The vasodilatation is one aspect of the patient's reaction to a specific life situation.

[As the authors point out, this group of patients, for several reasons, may not represent a random sample of sufferers from urticaria. The value of the work would have been enhanced if an attempt had been made to find out why these patients reacted to stress with a skin lesion and not with some other somatic change.]
Desmond O'Neill

811. **Life Situations, Emotions, and Glaucoma**
H. S. RIPLEY and H. G. WOLFF. *Psychosomatic Medicine* [*Psychosom. Med.*] **12**, 215–224, July–Aug., 1950. 5 figs., 20 refs.

To test the hypothesis that attacks of glaucoma may be precipitated by emotional tension, 18 patients with primary glaucoma were submitted to psychiatric investigation. There were 13 women and 5 men; the age range was 27 to 75 years. The patient's life history and emotional reactions were correlated with the course of the disease over periods of from 10 months up to 7 years. Intraocular pressure was measured at interview with the tonometer, and recorded on the McLean scale.

In all the patients there was a history of difficulty in personality adjustment. The most frequent manifestations were mood fluctuations, excessive anxiety, and hypochondriacal tendencies. Although no definite psychasthenic neurosis was observed, compulsive traits, such as conscientiousness and perfectionism, were common. Only in 4 patients had there been particular concern with the eyes before the development of glaucoma. Most of the patients had other bodily symptoms which seemed to be related to emotional tension. Interpersonal relationships, in the main, were unsatisfactory.

In every patient the onset of symptoms of glaucoma had been associated with a frustrating life situation which aroused anxiety, anger, or depression. It was repeatedly found that increased severity of eye symptoms, and elevation of intraocular pressure, coincided either with accentuation of an already existing frustration or with the development of new threats to the patient's security. When the patient was more contented and relaxed pressure was lower and symptoms receded. During interviews it was possible to demonstrate definite changes in intraocular pressure accompanying changes in emotional reaction. No specific situation or emotional reaction was found to be common to all the group. Elevations of intraocular pressure accompanied states of anxiety, anger, and depression, and, in a few instances, joyful exhilaration. In 9 patients changes in level of

blood pressure corresponded to those of intraocular pressure; in one, both blood pressure and intraocular tension were labile, but they were not correlated.

Although in those whose personality patterns were fixed, such as the elderly patients, psychotherapy had a limited value, it may be of some help in improving general adjustment to life, and in tiding the patients over periods of unusual stress.

[Other possible contributory factors in the aetiology of glaucoma are not sufficiently considered in this study. No family histories are given.] *Desmond O'Neill*

812. **Measures of Stress Responsivity in Younger and Older Men**

G. PINCUS. *Psychosomatic Medicine* [*Psychosom. Med.*] **12**, 225–228, July–Aug., 1950. 3 figs., 8 refs.

Two groups of normal healthy adult men were given four stress tests: the glucose tolerance test, pursuit meter test, targetball frustration test, and an adrenocorticotrophin test. The younger group contained 54 subjects, aged 19 to 43, with a median age of 32; the older group contained 30 men aged 61 to 92, with a median age of 77. Biochemical measurements were made on blood and urine specimens taken in the morning under basal conditions (pre-stress values), at 1¼ hours after the inception of the test (stress values), and at 3¼ hours (post-stress values). Determinations were made of those constituents which were considered to reflect adrenal cortical activity.

When the urinary variables (17-ketosteroids, neutral reducing lipids, potassium, sodium, uric acid) were calculated in terms of the creatinine output, no significant difference was found in the basal (pre-stress) output rate, except that the 17-ketosteroid excretion was higher in the younger group. Individual responsivity was assessed by means of a total response index (TRI), calculated for each subject from the percentage changes in urine composition over the pre-stress values, together with a weighted lymphocyte percentage change. While the younger men showed consistently higher mean TRI values, the differences are not significant for any single test. It would appear that adrenocortical responsivity to acute stress is very little diminished in the older men who were examined in this study. *Desmond O'Neill*

813. **Recurrent Herpes Simplex. A Psychiatric and Laboratory Study**

H. BLANK and M. W. BRODY. *Psychosomatic Medicine* [*Psychosom. Med.*] **12**, 254–260, July–Aug., 1950. 10 refs.

This paper is the report of a psychiatric survey of 10 patients with recurrent herpes simplex, 6 being men and 4 women, with an age range of 19 to 48 years. One of these was a schizoid character, a passive person in a state of violent rebellion, who could not be treated. The other 9 showed remarkable similarities in personality pattern. There was no resistance to psychiatric investigation, and the patients were anxious for help. They had noticed a relation between emotional upset and the occurrence of attacks of herpes. The prevailing pattern was that of a " good " and " pure " person who wished to follow the path of righteousness and avoid anything wicked, and who was passive, submissive, and eager to please. All made a rapid positive transference to the therapist, and all were ready to respond with obedience, in order to satisfy a need for approval. Emotional immaturity was outstanding. In 2 patients cancellation of an appointment with the therapist led to an attack of herpes within 24 hours. Improvement in the herpes was observed at an early stage in psychotherapy, and brief treatment seemed to be sufficient to control it, even when attacks had been almost continuous. Freedom from attacks was maintained over a follow-up period of many months. *Desmond O'Neill*

TREATMENT

814. **Effect of Insulin Hypoglycemia on Eosinophiles and Lymphocytes of Psychotics**

S. Y. TSAI, A. BENNET, L. G. MAY, and R. L. GREGORY. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 782–784, Aug., 1950. 15 refs.

The induction of insulin hypoglycaemia in 8 patients with schizophrenia caused a fall in the numbers of circulating eosinophils and lymphocytes similar to that produced by the injection of 11 : 17-oxysteroids. The fall was maximal 4 to 8 hours after insulin administration and 2 to 4 hours after the lowest blood glucose level was found. When glucose was given concurrently with insulin, and hypoglycaemia thus prevented, the blood changes did not occur. It is thought that these changes result from the release of adrenaline induced by hypoglycaemia.

A. C. Crooke

815. **Frontal Lobotomy. Neuroanatomical Observations**

P. I. YAKOVLEV, H. HAMLIN, and W. H. SWEET. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath. exp. Neurol.*] **9**, 250–285, July, 1950. 22 figs., 24 refs.

Extensive post-mortem histological studies were made in 6 cases in which prefrontal lobotomy had been performed at periods before death varying from 11 days to 32 weeks. As a rule the orbito-mesial quadrants of the frontal lobes were severed, involving the cingulate gyrus, while the dorso-lateral or convexal quadrants were largely spared. In the 4 cases in which the patient survived more than 2 months after operation the most conspicuous finding was the bilateral degeneration in the mesial or juxtacaudate part of the anterior limb of the internal capsule, in the subthalamic region, and in the rostro-mesial quadrants of the pons. The authors believe that the degeneration of the anterior thalamic radiations and nuclei has been stressed by other workers to the exclusion of the even more obvious degeneration of the far greater mass of efferent projections which connect the frontal lobes to all the levels of the neuraxis " in series " and " in parallel ". The findings in 3 of these cases indicated the presence of an atrophic process before the operation, which in one case was severe.

Radiographic studies should therefore always be carried out before undertaking lobotomy, especially in cases of schizophrenia of long standing. "Parasurgical" necrosis was greater with the aspiration needle than with the blunt leucotome. *W. H. McMenemey*

816. **The Psychology of Insulin Coma Treatment**
R. D. SCOTT. *British Journal of Medical Psychology* [*Brit. J. med. Psychol.*] **23**, 15–44, 1950. 5 figs., 4 refs.

The author attempts to explain the effects, in cases of schizophrenia, of insulin shock treatment in terms of Jungian psychology. His method of study, illustrated in detail by a description of 2 cases, consists of following the psycho-pathology of each schizophrenic patient in three successive settings: in the outside world, in the admission ward, and in the insulin ward. The atmosphere of the insulin unit and the daily routine of treatment tend to develop a positive group relationship, and the aim is to strengthen it further by weekly meetings and discussions. For the study of psycho-pathological mechanisms, the most important stage is that of emergence from coma. The patient's utterances during his gradual return to consciousness show a transient activation of psychosis in which paranoid fantasies are projected on the medical and nursing staffs. The insulin experiences indicate a fear of death and a threat to physical existence. Instinctive self-preservation forces are mobilized and the patient, while regaining consciousness, "gets out of the centre of the psychosis" by forming compulsive dependence on the staff, who represent a collective type of authority. Later, a true personal relationship is formed.

The whole process of coming round from "nearness to death" is considered to be psychologically closely related to primitive initiation ceremonies. The author discusses some of these initiation rites and their cultural development; they all have in common a danger to life and an ordeal through which the subject has to pass. A number of such experiences was described by schizophrenics undergoing insulin coma and, in view of their uniformity, the author believes that they belong to the racial unconscious and form a collective archetype. The shock treatment acts by activating these unconscious paterns and, by initiation and rebirth, facilitates a better contact with reality. Some practical suggestions for the management of insulin treatment, based on this hypothesis, are mentioned and the results of treatment are also briefly discussed.

[This interesting paper should be read in full, although there will be many who will disagree with this analytical interpretation of insulin treatment.] *J. T. Leyberg*

817. **L.S.D.25 as an Aid in Psychotherapy. (Preliminary Report of a New Drug)**
A. K. BUSCH and W. C. JOHNSON. *Diseases of the Nervous System* [*Dis. nerv. Syst.*] **11**, 241–243, Aug., 1950. 2 refs.

D-Lysergic acid diethylamide ("L.S.D.25") by mouth produces a mild toxic state. Since patients sometimes verbalize their conflicts during a toxic delirium, L.S.D.25 was given to 29 mental patients to facilitate obtaining information about their basic conflicts.

The drug is given orally in a solution of 20 μg. per ml. The average effective dose for men is 2·0 ml., for women 1·5 ml. Toxic effects begin in ½ to 1½ hours, and the effect is maximal 2 to 2½ hours, after administration. Symptoms persist on the average for 4 hours, in some cases 8 hours. Effects are both physical and mental. Physical effects include gastric distress, nausea and occasional vomiting, muscle tremors and twitching, dizziness, dilatation of the pupils and occasional hallucinatory flashes of light, chilliness, and tachycardia. The main mental effect is excitement, shown both by increase in movement and responsiveness and by greater verbal expression of the content of the illness.

The drug was tried on 29 patients at the St. Louis State Hospital; 20 were suffering from schizophrenia, 5 from neuroses, 3 from mania, and 1 from paranoia. Irrespective of their illness, most of these patients had tried to form personal relationships with the staff. Because of this, it was decided to try the drug on a group of 8 (included in the 29) who were already receiving psychotherapy, namely, the 5 with psychoneuroses and 3 with catatonia. The course of the illness was favourably influenced in all cases. Significant experiences of the past were re-lived and, in some cases, re-evaluated in more realistic terms. *J. P. Dewsbery*

818. **Trial of a New Synthetic Curarizing Drug, "336 H.C.", in Electric Convulsion Therapy.** (Essai d'un nouveau curarisant de synthèse 336 H.C. dans la technique de l'électrochoc sous curare)
J. DELAY, J. THUILLIER, and R. THEVENET. *Thérapie* [*Thérapie*] **5**, 109–114, 1950. 10 refs.

The effect in electric convulsion therapy (E.C.T.) has been studied of a new synthetic curarizing substance, "336 H.C.", which is said to be 66 times less toxic and 15 times less active than D-tubocurarine in animal experiments. It is the diiodoethylate of N : N′-bis-(piperidylethyl)piperazine and was used mainly in 20% solution. The required dose for each patient is injected intravenously over a period of one minute. Muscles are paralysed in the following sequence: eyelids, neck, tongue and pharynx, upper and lower limbs. Curarization is maximal after 3 or 4 minutes and the shock current should not be given before the third minute. After 3 minutes respiration is reduced by partial intercostal and diaphragmatic paralysis, but 336 H.C. does not cause any fall in blood pressure. The hypertension usually seen after E.C.T. without curarization is reduced when 336 H.C. has been given, probably because of the oxygen insufflation used as a routine to prevent anoxia. Although the muscular relaxation produced is less, 336 H.C. appears to have an advantage over D-tubocurarine in exerting some sedative effect, so that the patient is less anxious, or even euphoric. To assist rapid recovery, both neostigmine and oxygen have been given routinely. In common with other curare-like agents, 336 H.C. causes a considerable increase in bronchial secretion, which can be reduced by premedication with atropine. When required, a hypnotic is given after the curarizing substance. Under such conditions there may be a fall in blood pressure of up to 30 mm. Hg, and a higher shock current is required. *Derek R. Wood*

Infectious Diseases

VIRUS INFECTIONS

819. **Progress in the Treatment of Trachoma with Chloromycetin (Chloramphenicol)**
M. J. PIJOAN, E. H. PAYNE, and J. DINEEN. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **30**, 677–680, Sept., 1950. 17 refs.

Chloramphenicol was given to 6 adults and 8 children with trachoma. Children were given 1·5 g. daily for 3 to 4 days: the adults were given 3 g. as a first dose followed by 1·5 g. daily for 3 or 4 days. Apart from 2 adults who had some residual photophobia the conjunctivitis cleared and the lesions healed in all cases.
G. M. Findlay

820 (*a*). **Probable Transmission of Viral Hepatitis by Ultraviolet-irradiated Plasma. Report of Three Cases**
N. ROSENTHAL, F. A. BASSEN, and S. R. MICHAEL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 224–226, Sept. 16, 1950. 9 refs.

820 (*b*). **Hepatitis following the Use of Irradiated Human Plasma**
R. N. BARNETT, R. A. FOX, and J. G. SNAVELY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 226–228, Sept. 16, 1950. 3 figs., 2 refs.

820 (*c*). **Homologous Serum Jaundice Associated with Use of Irradiated Plasma. A Preliminary Report**
G. JAMES, R. F. KORNS, and A. W. WRIGHT. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 228–229, Sept. 16, 1950. 9 refs.

These three communications all deal with the same subject and show that, as practised, exposure of plasma to ultraviolet light does not inactivate the hepatitis virus. Altogether 16 cases of hepatitis are described, 2 of them fatal, following the injection of irradiated plasma. There is thus no reliable method as yet for inactivating hepatitis viruses in plasma, serum, or whole blood.
G. M. Findlay

821. **Infective Hepatitis in North Africa**
H. J. A. RICHARDS. *Journal of the Royal Army Medical Corps* [*J.R. Army med. Cps*] **95**, 103–118, Aug., 1950. 3 figs., 15 refs.

A survey is made of the incidence of infective hepatitis among British troops stationed in North Africa between July, 1947, and February, 1950. By recording the case incidence graphically, it is shown that the disease was epidemic, there being a regular wave each autumn and early winter, with a peak incidence during October or November of about 4 or 5 per 1,000. It is concluded from analysis of the detailed case histories that the disease was probably spread by oral ingestion of the virus. The vehicle of transmission might be food, water, improperly washed crockery and cutlery, or even papers and documents in offices. The disease attacked, to a disportionate degree, officers, all ranks of headquarter and support companies, and those who worked in offices or stores. It is suggested that the greater susceptibility of officers is partly due to the fact that they are likely to have been less exposed to the disease in infancy and childhood and therefore reach adult life with little immunity. Prevention of the disease is dependent on raising the sanitary standards, particularly as regards food hygiene and the adequate washing of crockery.
Geoffrey McComas

822. **Recurrent Herpes (Cytology of Vesicle Fluid)** (Herpes recidivante (citologia del liquido de su vesicula))
A. TELLO ORTIZ. *Actas Dermo-sifiliográficas* [*Act. dermo-sifiliogr., Madr.*] **41**, 831–834, June, 1950. 4 figs. 16 refs.

The cell picture of vesicle fluid in recurrent herpes is essentially the same as that in herpes simplex, with the same evolution of the elements towards eventual destruction by lysis. Eosinophils and mast cells are constantly present in recurrent lesions, and this, together with the fact of recurrence in the same area, suggests a state of allergy to the virus. This finding may be of importance in the planning of treatment.
James Marshall

See also Section Psychiatry, Abstract 813.

823. **A Disease Epidemic in Iceland Simulating Poliomyelitis**
B. SIGURDSSON, J. SIGURJÓNSSON, J. H. SIGURDSSON, J. THORKELSSON, and K. R. GUDMUNDSSON. *American Journal of Hygiene* [*Amer. J. Hyg.*] **52**, 222–238, Sept., 1950. 5 refs.

In the winter of 1948–9 an extensive epidemic occurred among the inhabitants (6,900) of the town of Akureyri on the north coast of Iceland. The disease affected the central nervous system. The first case was seen on Sept. 25, 1948, and from then on, until Feb. 19, there were 465 cases in the town and 23 in the surrounding countryside: 137 of these cases were paralytic. Two other towns were involved: in Isafjördur (population 3,020) there were 206 cases from January to April, 1949, and in Saudárkrókur (population 2,400) 147 from December, 1948, to February, 1949. Multiple cases in households were frequent, and schools, except for the elementary school, were heavily involved: 145 cases occurred among 679 students attending the senior schools, the majority of these students being 15 to 19 years of age. The disease was characterized by pains in the back and nape of the neck accompanied by low fever. Paraesthesiae and hyperaesthesia were common, and approximately 28% of the patients showed muscular paresis, usually slight, but in some cases severe. Not infrequently the fever lasted some weeks, and relapses of fever with pareses and sensory changes were noticed some weeks after the primary attack. The slightest physical exertion or exposure to cold

aggravated the symptoms and brought on new manifestations of the disease. Patients with less severe paresis recovered fairly well, but some in whom paresis was severe have remained seriously disabled. Polyarthritis developed after the illness in a number of cases. Sleeplessness and loss of memory were common complaints. There was an increase in protein and cells in the cerebrospinal fluid. No deaths occurred, so that the pathological changes are unknown.

It was not possible to transmit the disease to animals so that poliomyelitis could be excluded; Coxsackie infection was ruled out, and the sera from convalescent patients failed to show immune bodies against St. Louis, Japanese B, or east and western equine encephalomyelitis viruses. There was no evidence that the disease was transmitted by food, milk, or water, and sanitation was good in the towns in which the disease occurred. Insects as possible vectors were unlikely. The evidence therefore suggests that the infection was transmitted by direct contact. It would seem possible that the causal agent was either an abnormal poliomyelitis virus of very low virulence or a new neurotropic virus. The clinical symptoms, however, were not those observed in any known outbreak of poliomyelitis.

G. M. Findlay

POLIOMYELITIS

824. **Observations on Serological Epidemiology. Antibodies to the Lansing Strain of Poliomyelitis Virus in Sera from Alaskan Eskimos**

J. R. PAUL and J. R. RIORDAN. *American Journal of Hygiene* [*Amer. J. Hyg.*] **52**, 202–212, Sept., 1950. 5 figs., 10 refs.

It is commonly believed that Eskimos are less exposed to poliomyelitis than other populations. Sera were therefore collected from an area on the north coast of Alaska where poliomyelitis is known to have occurred in 1930, but there is no reference to its having been present before or since that date. The neutralizing-antibody tests against the Lansing virus showed that nearly all the natives tested from two villages who were below the age of 20 had no antibodies, whereas of those aged 20 and over, about 80% had antibodies in their sera. These findings suggest that antibodies to the Lansing strain of poliomyelitis virus persist for 20 years.

G. M. Findlay

825. **Dual Antibody Response to Coxsackie and Poliomyelitis Viruses in Patients with Paralytic Poliomyelitis**

J. L. MELNICK and A. S. KAPLAN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 812–815, Aug., 1950. 4 refs.

Because the simultaneous excretion of both Coxsackie (C) and poliomyelitis viruses from the intestinal tract of man during illness and health and the simultaneous recovery of these two viruses from flies trapped in poliomyelitis areas have been demonstrated, it is important to determine whether the host is infected by both these agents or whether one passes passively through the alimentary tract. In this paper the authors give evidence that paralytic patients excreting both viruses respond serologically with antibodies to both of them.

Samples were taken from 48 consecutive patients during a severe epidemic of poliomyelitis in Easton, Pennsylvania, in 1949, and both C virus and poliomyelitis virus were isolated from 15. Two paralytic cases were selected for more detailed study. The titre in monkeys of poliomyelitis virus in the stools of each patient was 10^{-2}, so that it was possible to use this original human source as a source of virus for the neutralization test. The titre of C virus in newborn mice was 10^{-1} and 10^{-3} respectively, and the original human-source virus and also mouse-passage virus were used for neutralization tests. Sera were used in serial three-fold dilutions. A supernate with a concentration of 10^{-1} was put up with an equal volume of serum at dilutions of 1 in 10, 1 in 30, 1 in 90, and 1 in 270. After incubation at room temperature for 2 hours each serum–virus mixture was inoculated into 3 monkeys and into at least 8 newborn mice. With mouse-passage virus C, 100 ID50 was added to the serum dilutions.

The highest serum dilution in the first patient which neutralized C virus on the third day of the disease was 1 in 10; by the 32nd day it was 1 in 90. These titres, calculated on the basis of the serum dilution which protects 50% of the animals, were 1 in 50 and about 1 in 300 respectively. With mouse-passage C virus, acute-phase serum was negative, but the convalescent serum titres were 1 in 50 for complete neutralization and 1 in 150 for 50% protection. Response of the first patient to poliomyelitis virus was shown by a rise in titre; during the acute phase a 1 in 10 serum dilution completely neutralized the patient's virus, while in the convalescent stage it could not do this even at a dilution of 1 in 270. On the basis of a 50% protection of animals this titre thus increased from 1 in 20 to a figure greater than 1 in 270. The serum of the second patient showed comparable increases in titre.

Titration of the paired sera of each patient against 100 ID50 of the Easton-2 strain of C virus gave the same results as those obtained against the mouse-passage strains from the 2 patients. Because this Easton-2 strain is antigenically identical with Dalldorf's type-1 strain, it appears that the strains from both patients were of this latter type.

The authors conclude, from these results and from the discovery of both viruses in the stools of 13 other patients in this epidemic, that failure to detect poliomyelitis virus in a paralytic patient excreting C virus should be regarded as due to a technical cause. It does not necessarily mean that C virus caused the paralytic lesion and, until it is proved otherwise, the paralytic signs should be ascribed to poliomyelitis virus. The occurrence of dual infection with both viruses is, however, too frequent to be regarded as a coincidence and the authors ask whether the infection with poliomyelitis virus might not have been mild without the superimposition of C-virus infection. The possibility that C-virus infection may be one of the predisposing factors that turn a non-paralytic into a paralytic poliomyelitic infection is also suggested.

G. Lapage

826. **Respiratory Studies in Paralytic Poliomyelitis**
R. B. BOURDILLON, E. DAVIES-JONES, F. D. STOTT, and L. M. TAYLOR. *British Medical Journal* [*Brit. med. J.*] 2, 539–547, Sept. 2, 1950. 6 figs., 29 refs.

This paper is based on observation of patients suffering from poliomyelitis with respiratory paralysis and treated in tank respirators at the Western Hospital, Fulham, London, and on laboratory studies at the M.R.C. Electromedical Research Unit, Stoke Mandeville Hospital.

The authors chiefly studied the effects on tidal air and minute volume of varying respirator suction pressures and stroke frequencies. They also studied the effects of varying the patient's posture in the respirator, and the changes occurring in convalescent patients during and after weaning from it. They measured tidal air with a spirometer of the water-seal gasometer type. Nine cases were studied, 4 in some detail. Four healthy subjects were also included in the series.

About 600 measurements of tidal air were made and correlated with the amount of negative pressure in the Both and Drinker respirators. The results showed wide variations, both between different persons and from day to day in the same person. It was found easy to obtain smooth curves relating negative pressure to tidal air if the pressure was altered quickly. Healthy subjects showed less resistance to the respirator action than did patients. The normal volumes of tidal air should be adequate for respirator patients, unless there is high temperature or obstruction by mucus. Thus tidal air should not exceed 600 c.cm. and not be less than 400 c.cm. for a respiration rate of 15 cycles per minute; a suction pressure of −12 to −15 cm. is likely to be of the right order and should be tried at first, although higher negative pressures may be required in severe cases. Oxygen and CO_2 in blood (or alveolar CO_2) should be measured if possible, although the patient's comfort may be a useful guide in the absence of measurements.

Positive pressures did not appreciably increase the tidal air, but were thought to be of use in maintaining flexibility of the chest, assisting circulation in the lungs and liver, and aiding coughing.

Increase of stroke frequency in healthy subjects caused a fall in tidal air; 20 cycles a minute (the minimum frequency of the normal Both apparatus) was uncomfortably fast. Speeds of 12 to 16 cycles were preferred. Although febrile patients may require higher frequencies, low frequencies in afebrile cases are advantageous. Tidal-air measurements in patients removed from respirators showed how low a value could be tolerated by a wasted convalescent patient. The reserve air in patients with greatly damaged respiratory muscles is very low, and there is no margin for emergencies such as acute respiratory infections.

Postural drainage is often of great importance, especially in the bulbar type with accompanying pharyngeal paralysis. The advantages of nursing patients in the prone position in respirators are pointed out. This position greatly facilitates drainage owing to the inclination of the trachea, and less tilting of the respirator is required. Some modification of the sloping front of both Drinker and Both respirators is needed to make this change of posture easier. Tidal air is not decreased by adoption of the prone position.

Hyperventilation can easily be produced in tank respirators in healthy subjects. With patients, pressure was generally adjusted to the lowest value at which the occupant felt comfortable and no signs of overventilation were detected. The need for putting patients early into respirators to rest the respiratory muscles is stressed.

If a spirometer is not available to measure the vital capacity, a rough estimate of the first onset of respiratory weakness can be formed by finding how many numbers a patient can count aloud in one expiration. In matching respirator frequency to the patient, the unaided frequency of respiration should be first noted and the machine adjusted to the same frequency when this is not excessive. To guard against the risk of hypoxia blood oxygen should be estimated if possible. In the absence of such facilities it seems wisest to choose a minute volume rather greater than the optimum theoretical value for a patient at rest. Many patients benefit from the use of oxygen in the early stages; some auxiliary apparatus, such as the Oxford inflator, may be required when the patient is out of the tank respirator for nursing attention.

Further alterations to the Both respirator are suggested, the most important being the provision for running at speeds lower than 20, an alarm system for calling attention to cessation of adequate pressure changes, and the addition of a metal pressure gauge.

[This important paper is likely to improve greatly the design and use of the tank type of breathing machine.]

J. V. Armstrong

827. **Clinical Management of Acute Poliomyelitis**
E. SMITH, D. J. GRAUBARD, J. FALCONE, T. B. GIVAN, P. ROSENBLATT, and A. FELDMAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144,** 213–218, Sept. 16, 1950. 1 fig., 13 refs.

When searching for the cause of pain, spasm, and vasomotor instability during the acute and subacute stages of poliomyelitis, the authors were impressed by the regular occurrence of lesions in the sympathetic ganglia in fatal cases. They believe that the pressure of these lesions, together with those of the internuncial and intermediolateral cell groups of the spinal cord and brain stem, may offer a rational explanation of the ischaemic pain and sympathetic instability of the disease.

This report describes the attempted control of these symptoms by the sympatholytic drug "priscoline" (2-benzyl-4 : 5-imidazoline) hydrochloride. This is an anti-adrenaline drug with a marked peripheral vasodilator action. The 663 patients treated were selected from a series of 847 during the 1949 season because they had pain, muscle tenderness, arterial tenderness, or muscle spasm, or any combination of these. The drug produced vasodilatation and increased blood flow, as shown by oscillometric increase in blood volume in the extremities in 61 cases. Only cases of spinal disease were treated, a small trial having shown that encephalitic, bulbar, and bulbospinal disease and cases in respirators were not affected by the treatment. The dose varied according to age from 5 to 50 mg. or more, being increased until flushing was produced. The dose causing flushing was main-

tained 3-hourly during the day and 4-hourly during the night for an average of 11 days. The drug was given at first intramuscularly and, when pain and muscle spasm subsided, orally in rather higher dosage. The effects produced were a rise in skin temperature, frequently nausea and vomiting, flushing, sensation of warmth, diaphoresis, palpitation occasionally, and rigors, paraesthesiae, and diarrhoea rarely. The outstanding result, however, was an improvement and the appearance of a sense of well-being within 30 minutes of administering the effective dose. Pain disappeared, muscle tightness diminished, cold, clammy skin became warm, and the patient was able to sleep comfortably. The nursing staff were relieved of the tremendous load that they would have had to bear if treatment with hot packs had been used. The authors consider that, at the very least, further investigation of the use of this and other sympatholytic drugs is indicated. *H. Stanley Banks*

828. **Poliomyelitis and Tonsillectomy: a Review of the Literature for the Oto-rhino-laryngological Society of New South Wales**
R. E. DUNN. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 243–246, Aug. 12, 1950.

BACTERIAL INFECTIONS

829. **The Chronic Typhoid Carrier. III. Therapy with Antagonistic Bacillus, Antibiotics and Sulfonamides**
J. A. VAICHULIS, A. LITTMAN, A. C. IVY, G. ZUBOWICZ, and R. KAPLAN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **33**, 361–370, Aug., 1950. 10 refs.

In the typhoid carrier, if the infection is predominantly in the gall-bladder and accompanied by the presence of demonstrable stones, the only really effective treatment is surgical removal. If the infection is predominantly in the gall-bladder but stones are absent, combined treatment with penicillin, sulphonamides, and tetraiodophenolphthalein will usually effect a cure in a few weeks. The most serious and difficult form of infection and the one that has hitherto given rise to most trouble and caused spread of infection in most epidemics is in the chronic typhoid carrier with an intestinal reservoir of infection. Such infections are singularly obstinate and difficult to treat. The present authors give an account of how such infections can be treated by the oral administration of an emulsion of bacteria found to be antagonistic to the typhoid organisms. These antagonists are related to *Bacillus subtilis* and the emulsion is in the form of a rather unpalatable syrup which, however, can be taken without much disturbance if " served cold ".
G. F. Walker

830. **A Comparison of " Symptomatic Treatment ", Gamma Globulin, and Penicillin in the Treatment of Scarlet Fever**
L. WEINSTEIN and S. F. POTSUBAY. *Journal of Pediatrics* [*J. Pediat.*] **37**, 291–306, Sept., 1950. 20 refs.

A series of 255 cases of scarlet fever were divided into three groups, the alternate case method being used: 102 patients were given symptomatic treatment, consisting of rest in bed, throat irrigations, and so on; 103 patients were given one intramuscular injection of gamma globulin (20 to 60 ml.); 50 patients were treated with penicillin (15,000 units intramuscularly every 3 hours for 10 days).

Gamma globulin caused a marked amelioration of the toxic signs and symptoms, rapid fading of the rash, and disappearance of headache, nausea, vomiting, and general muscle pains. There was no significant alteration in the incidence of complications. The injections caused continued pain in some patients, necessitating the use of analgesics.

Penicillin markedly shortened the course of the acute phase, rapidly eradicating the causative organisms. It usually prevented suppurative complications and the appearance of the carrier state. It is concluded that penicillin is the agent of choice. *R. S. Illingworth*

831. **The Initial Reduction in Isohaemagglutination in Toxic Diphtheria in Children.** (Der initiale Isohämagglutinationssturz bei toxischer Diphtherie des Kindes)
T. HOCKERTS and J. STRÖDER. *Archiv für Kinderheilkunde* [*Arch. Kinderheilk.*] **140**, 82–90, 1950. 2 figs., 35 refs.

In severe, toxaemic cases of diphtheria in children the authors found a lack of isohaemagglutinins against erythrocytes of groups A and B. This phenomenon occurred during the first few days of illness and tended to be compensated during the later stages by a comparatively high titre. In mild and moderate cases of diphtheria no change in the isohaemagglutinin titre was observed. Similar results were obtained when normal serum was mixed *in vitro* with diphtheria or other bacterial toxins, the titre of isohaemagglutinins falling to low figures after the addition of the toxin.

The procedure of investigation *in vivo* consisted in making twice-weekly determinations of the isohaemagglutinin titre in the patients' serum. Haemolytic sera were rejected. Serum dilutions doubling from 1 in 4 to 1 in 1,024 were tested against 0·2 ml. of a 1·5% suspension of human erythrocytes, readings being taken after 2 hours' incubation at 35° C. Sera from patients belonging to blood-group A were tested against erythrocytes of group B and vice versa, while sera from patients of group O were tested against erythrocytes of groups A and B separately, and those from patients of group AB could not be tested at all. For the investigations *in vitro* the same serum dilutions were used, 0·17 ml. of toxin being added to the first tube before carrying out the dilutions. Readings were taken after 2, 4, 6, 8, 24, and 36 hours' incubation at 37° C. The amount of diphtheria toxin used (0·7ml.) corresponded to 12 M.L.D. —the dose supposed to be lethal for children—and to avoid varying the experimental conditions the same volume of toxin was used in testing the effect of tuberculin and the toxins of tetanus, dysentery, *Bacterium coli*, and staphylococci. In all these experiments a reduction of the isohaemagglutinin titre was observed when either purified toxin or sterile nutrient medium containing it was added to the serum. A reduction did not occur when the toxin was heated for 20 minutes at

56° C. or when antitoxin was added. [There does not appear to be any record of control experiments in which a heated nutrient medium was added to the serum.]

Inasmuch as the reduction of the anti-A titre is concerned this might be explained by the presence in the nutrient medium of a substance chemically related to the substance characterizing blood-group A, as reported by Holl and Schmidt. No such explanation is available in the case of blood-group B and the authors, after discussing various possibilities, are careful not to commit themselves to any opinion on the nature of the phenomenon which they have observed and described.

K. S. Zinnemann

832. **Purified Toxoid Aluminium Phosphate ("P.T.A.P."). Report on Australian Field Trials**

E. F. MACKENZIE. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 473–475, Sept. 23, 1950. 2 refs.

This report deals with an investigation into the Schick-conversion rate after immunization against diphtheria with purified toxoid precipitated with aluminium phosphate (P.T.A.P.). The standard routine measures adopted consisted in: (1) Schick-testing all children without a toxin control. (2) Limitation of immunization to the Schick-positive children who had not been inoculated previously. (3) Administration of 0·5 ml. of P.T.A.P. as first, and 0·25 ml. as second dose subcutaneously into the deltoid region, first of the left and then the right arm. As some severe reactions occurred after the first dose the dosage was subsequently amended to 0·25 ml. for the first and 0·5 ml. for the second injection. (4) Administration of the doses at 6 weeks' interval. (5) Assessment of Schick conversion 8 weeks after the second injection.

Just short of 2,000 children were inoculated. In only 8 cases were moderate or severe reactions observed. Complete information was obtained of 1,554 Schick-positive children, of whom 99·8% were rendered Schick-negative. One dose only was given to 311 additional children, amongst whom the conversion rate was 96·7%. The author therefore advises against one-shot immunization with P.T.A.P.

[A flaw in this otherwise excellent report is the omission of controls in the initial Schick test.]

K. S. Zinnemann

833. **Cutaneous Diphtheria. Epidemiological and Dermatological Aspects of 365 Cases amongst British Prisoners of War in the Far East**

G. S. RIDDELL. *Journal of the Royal Army Medical Corps* [*J.R. Army med. Cps*] **95**, 64–87, Aug., 1950. 1 fig., 32 refs.

The author describes an outbreak of diphtheria among British prisoners of war in Japanese camps on Singapore Island between February, 1942, and February, 1943, and emphasizes the high incidence of cutaneous lesions, which occurred in 37·8% of all cases of diphtheria during this period.

Such lesions never developed on intact skin, and ulceration of the skin or scrotal dermatitis due to hypo-riboflavinosis frequently paved the way for diphtheritic infection. Involvement of the scrotum occurred as an acute inflammatory lesion with much general toxaemia, but with eventual healing. In the 167 uncomplicated scrotal cases the case fatality rate was 7·18% and the incidence of cardiac and neurological complications was 29·3%. The cutaneous lesions elsewhere were either membranous or non-membranous; in the cases in which there were no coincident faucial or nasal lesions the fatality rate was 1·33% and the incidence of neurological or myocardial complications was 28%. Supplies of antitoxin were scanty, and its use restricted to cases causing grave anxiety. In other cases treatment consisted of prolonged rest, local applications of various types, and the administration of "marmite" or "vegamite".

Geoffrey McComas

834. **Aureomycin in the Treatment of Pertussis: a Preliminary Report**

W. J. MILLER and J. E. ROSS. *Journal of Pediatrics* [*J. Pediat.*] **37**, 307–310, Sept., 1950. 1 ref.

Six patients with whooping-cough, 4 critically ill, were treated with large doses of aureomycin (350 mg. per kg. body weight per 24 hours) for 8 to 10 days. In 3 cases hyperimmune serum was given before aureomycin was used, and in one of these streptomycin was given intramuscularly for 18 hours before aureomycin administration started. Vomiting and cyanosis cleared in 3 to 5 days. Paroxysms persisted longer, but diminished steadily in frequency. All patients were virtually free from paroxysms in 7 to 10 days.

R. S. Illingworth

835. **Brucellar Spondylitis.** (Die brucellöse Spondylitis)

S. DI RIENZO. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **73**, 333–348, July, 1950. 20 figs.

The incidence of spondylitis in cases of brucellosis has been estimated at between 20% and 75%. Involvement of the spine was first observed in 1897.

Any part of the spine may become the site of a lesion, but most frequently the lumbar spine is involved (80%). Sacro-iliac joints are as frequently affected as is the lumbar spine. The lesion involves bones and soft tissues (spinal cord, nerves, meninges) equally. Lesions are generally multiple, but may be single, and confined to one vertebra or one intervertebral disk alone.

Symptoms vary greatly. Lumbar pain and muscular contracture are by far the most common. The pain is resistant to all common analgesic drugs and is not characteristic. The intensity of pain, which varies from case to case, does not necessarily correspond with the extent of the pathological changes, and does not indicate the site. Variations in intensity of pain are not related to the degree of fever. If a paravertebral abscess develops subacute peritonitis may follow.

Radiological examination must be preceded by careful preparation of the patient with adequate doses of castor oil, and with one or two ampoules of "pitressin" 30 minutes before the examination. In cases with peritoneal complications this is, of course, not practicable, and the accumulation of intestinal gas is neutralized by instructing the patient to breathe quietly during the exposure. A

fine-focus tube or a rotating-anode tube should be employed. Lateral films, both left and right, should be taken; they provide most information. Radiological abnormalities tend to lag behind clinical symptoms and pathological changes. In acute brucellosis the bones appear ill-defined, this appearance simulating a technical fault. In the chronic stage of the disease there is marked exaggeration of bone trabeculation, which is caused by osteoporosis. The lesion usually begins in the upper or lower vertebral epiphysis and early affects the anterior longitudinal ligament, and frequently also the nucleus pulposus. This characteristic appearance resembles Schmorl's nodes closely. Bone reaction enhances the appearance of exostoses. Erosions may appear anywhere in the vertebral body. In the later stages of the disease the intervertebral spaces begin to narrow. The vertebral bodies appear denser than usual, and bridging occurs between adjacent vertebrae. Appearances closely resemble those in Pott's disease. Radiological differential diagnosis is very difficult. The bone reaction in brucellosis is much more pronounced than that in tuberculosis, and lesions are much more destructive in the period of growth than in adult life. There are no pathognomonic radiological signs. Diagnosis is not possible on the evidence provided by a single examination; it is somewhat easier when progress is observed. The radiological pictures must fulfil the following requirements: (1) show multiple vertebral lesions; (2) show co-existing lesions in various stages; (3) show spontaneous tendency to repair.

The degree of bone destruction of the spine in brucellosis bears no relation to prognosis; large lesions may heal completely, very small ones may be associated with a grave general condition, ending in death. Large lesions of bone may cause complete incapacity of the patient. *L. G. Capra*

836. **The Choice of Treatment in Brucellosis.** (Orientamenti di terapia nella infezione brucellare)
A. LUCIANI and V. MERLINI. *Rassegna di Fisiopatologia Clinica e Terapeutica* [*Rass. Fisiopat. clin. terapeut.*] **22**, 323–346, May, 1950. 7 figs., 22 refs.

In this paper from the Medical Clinic of the University of Pisa the authors attempt to compare the efficacy of different methods of treatment for brucellosis, a disease which, in Italy, is becoming more frequent and more severe. In a series of 60 cases no less than 50 patients were moderately or seriously ill, and there was one death; there were nearly 3 males to every female, but all age groups were represented.

Vaccine in increasing doses of 50 to 1,000 million organisms given intravenously—a form of treatment largely ignored in other countries—was used, either alone or in combination with antibiotics, in 52 cases, and has a valuable place in treatment. It must, however, be given at the right time, and the severity of the illness may preclude its use in the early stages. Combined treatment with sulphadiazine and streptomycin should no longer be used, because of the toxicity of the drugs, the paucity of response, and the availability of newer and less toxic drugs. Aureomycin in total doses of 10 to 27 g. produces a constant effect in an average of 4·45 days, but relapses occur when the drug is used alone, and it is at present expensive. Chloramphenicol in a dosage of 3 g. daily for 4 to 8 days is more certain and produces a fall in temperature in an average of 5·75 days.

There are two objects in the treatment of brucellosis: (1) complete removal of the organism from the body, and (2) the establishment of a satisfactory immunological state in the patient. It seems improbable that the antibiotics at present in use will achieve the first of these conditions, yet they may obviate the need for the body to produce sufficient antibodies. It is rational, therefore, to use a combination of vaccine and antibiotics—of which chloramphenicol is the most satisfactory—to effect a complete eradication of the offending organisms. *A. Paton*

837. **Aureomycin Therapy in Abortus Fever.** (Aureomycintherapie des Morbus Bang)
E. STOFFEL. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **80**, 1005–1010, Sept. 16, 1950. 3 figs., bibliography.

The author records the effect of aureomycin in the treatment of infections with *Brucella abortus* at the Cantonal Hospital, St. Gallen, Switzerland. Of the 15 patients treated 11 were in the acute febrile phase and 4 in the apyrexial interval, while 5 cases presented serious complications. In all cases the therapeutic effect was most striking; fever was reduced in not more than 4 days, with rapid abatement of all signs and symptoms. In one case only was there a relapse, but this finally yielded to treatment after a total of 79 g. of the antibiotic had been given. Most noticeable was the rapidity with which complications such as osteomyelitis, spondylitis, and lymphadenitis subsided under treatment after various other therapeutic measures had failed.

The dosage of aureomycin was 2 g. daily, given by mouth in all cases, the total dose ranging from 14 to 30 g. A mild form of gastro-enteritis was commonly observed, though this never attained such severity as to necessitate withdrawal of the drug. In one case stomatitis and pruritus developed. Follow-up of these patients showed that all remained well several months after completing treatment. The author considers aureomycin greatly superior to any other drug or means of treatment in this disease. *Joseph Ellison*

See also Section Neurology, Abstracts 804–5.

838. **Chloromycetin in the Treatment of Cholera.** [In English]
R. N. CHAUDHURI, S. GHOSAL, and M. N. RAI CHAUDHURI. *Indian Medical Gazette* [*Indian med. Gaz.*] **85**, 398–400, Sept., 1950. 5 refs.

Gauld *et al.* (*J. Bact.*, 1950, **57**, 349) showed that chloramphenicol had an inhibitory action on the growth of *Vibrio cholerae*. In India the effects of the drug were tested on 10 patients with cholera while 10 other patients, alternating with those treated, served as controls. All patients were given the usual saline treatment for dehydration, which, in most cases, was severe. The average period of illness until treatment was started was 9 hours.

Among the treated patients 2 died, and of the controls one died. Chloramphenicol was given in spaced doses at the rate of 12 g. in 3 days. No difference in the clinical course of the disease was noted, but in patients receiving chloramphenicol vibrios had disappeared from the stools in 24 hours, whereas in controls they could be found in the stools up to the 7th day. *G. M. Findlay*

TUBERCULOSIS

839. **The Value of the Haemagglutination Reaction for the Diagnosis of Tuberculosis and the Control of Vaccination with B.C.G.** (Intérêt de la réaction d'hémagglutination pour le diagnostic de la tuberculose et le contrôle de la vaccination par le B.C.G.)
C. GERNEZ-RIEUX and A. TACQUET. *Revue de la Tuberculose* [*Rev. Tuberc., Paris*] **14**, 676–684, 1950. 1 fig., 6 refs.

The value of the Middlebrook–Dubos haemagglutination reaction in experimental and clinical tuberculosis was investigated by the authors, the original technique being used throughout in addition to modifications employing various tuberculin antigens. In rabbits vaccination with B.C.G. was followed regularly by positive haemagglutination to a moderately high titre during the first month, falling later to a lower level. After the intravenous infection of rabbits with 0·1 mg. of a bovine strain (Ravenel) of *Mycobacterium tuberculosis* a positive haemagglutination reaction was elicited to a high titre before the appearance of allergy. Streptomycin treatment, which is very effective in the rabbit, caused a marked fall in the haemagglutination titre.

Sera from animals with significant naturally-acquired lesions of bovine tuberculosis gave positive haemagglutination reactions in 80% of cases. No agglutination occurred in the serum of 96% of 233 clinically and radiologically healthy human subjects, whereas sera from 487 tuberculous patients gave positive haemagglutination reactions in 77% of cases. After B.C.G. vaccination in adolescents and children the serological response was variable. Compared with complement-fixation reactions for tuberculosis the Middlebrook–Dubos reaction gave approximately 10% more positive results in tuberculous patients and only 5% of non-specific reactions as against 25%. It is hoped that by improvements in the technique and the nature of the antigen the specificity of the reaction may be further increased so that the test may be useful in early diagnosis, and possibly in the control of B.C.G. vaccination. *E. Nassau*

840. **The Pathogenesis of Tuberculosis in Mice Infected Intravenously with Human Tubercle Bacilli; the Use of Mice in Chemotherapeutic Tests**
G. T. STEWART. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **31**, 5–13, Feb., 1950. 7 figs., 7 refs.

The effect of the intravenous injection of various doses [measured as moist weight] of virulent and less virulent strains of *Mycobacterium tuberculosis* in white mice was observed; the inocula were suspensions from 17-day cultures on Loewenstein's medium. Survival time, weight change, and the rating on a pathological assessment were the chief criteria. With a dose of 0·75 mg. of human virulent strain 905, the mice developed proliferative, followed by necrotic, pulmonary lesions containing increasing numbers of bacilli, and died in 3 to 5 weeks; the predominant cells were large and small mononuclears. With 0·02 mg. of the same strain the mice died in 3 to 14 weeks, with necrotic pulmonary lesions in those dying early and proliferative lesions in those dying later. With 0·01 to 0·0004 mg. of this strain the survival time was even longer and the lung lesions were mainly or entirely proliferative, with many " foam-cells " in the alveoli. When mice were infected with 0·75 mg. of the low-virulence strain M, death occurred in 4 to 14 weeks; the pathological evolution resembled that after the smaller inocula of the virulent strain, with conspicuous proliferative changes and foam-cell reaction.

The main conclusion is that lowering either of the virulence or of the dose of the inoculum of *M. tuberculosis* was associated with longer survival with substitution of proliferative for necrotic lesions at death, and with an alveolar foam-cell reaction; the infection was nevertheless always progressive and unremitting. Hence " chronic " disease differed from " acute " mainly in degree; in both types true tubercles, giant cells, caseation, fibrosis, and cavitation were notably absent. Previous vaccination of mice with small doses of strain 905 made them more resistant to reinfection with large doses of this strain, as evidenced by longer survival and a higher proportion of proliferative lesions, though fibro-caseous changes and remission still did not occur. From these observations on the pathogenesis of experimental mouse tuberculosis, the author has devised a scheme for the pathological assessment of the effects of chemotherapy.

[The conclusions on pathogenesis, particularly the unremitting progression after even the smallest doses, should probably be taken to apply only to the strains of mice and bacilli here used.] *P. D'Arcy Hart*

841. **Enhancing Effect of Cortisone on Tuberculosis in the Mouse**
P. D'ARCY HART and R. J. W. REES. *Lancet* [*Lancet*] **2**, 391–395, Sept. 23, 1950. 4 figs., 14 refs.

The authors produced non-progressive tuberculosis in mice by injecting small doses (0·0006 mg.) of tubercle bacilli suspended in Dubos's medium. Advantage was taken of the stability and chronicity of the infection to assess the effect of cortisone on experimental murine tuberculosis.

In one experiment cortisone was administered in a dose of 0·5 mg. daily to 11 animals infected 9 weeks previously. Eight of these died within 22 days from the commencement of the course; at necropsy, the lung lesions were seen to be extensive and necrotic, and contained large numbers of tubercle bacilli. No death occurred in a control group of infected mice not treated with cortisone. When killed after 22 days the control animals showed minimal lung lesions with scanty tubercle bacilli.

Similar results were obtained in a second experiment in which 36 infected and 10 non-infected animals were

used. Non-infected mice treated with cortisone remained well, as did tuberculous mice not treated with cortisone. All cortisone-treated tuberculous mice sickened and several died from advanced pulmonary tuberculosis. The larger the dose of cortisone, the sooner did death supervene.

A more acute type of infection was produced in a group of 30 mice by injecting 0·06 mg. of tubercle bacilli. Ten received 0·5 mg. of cortisone daily from the day of infection, and the remainder served as untreated controls. Again there was a striking difference in survival time and mortality rate between the treated and untreated mice. The untreated group survived the infection for 14 to 24 days; all the treated animals sickened during the first week and died 15 days after infection. The tuberculous foci in these treated animals were widespread, necrotic, and teeming with tubercle bacilli.

The authors believe that cortisone aggravates tuberculosis in the mouse by lowering the animal's high natural resistance to the disease. The mechanism of this effect is obscure. *G. B. Forbes*

842. **Tuberculous Meningitis**

H. CAIRNS, H. V. SMITH, and R. L. VOLLUM. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 92–96, Sept. 9, 1950. 2 figs., 15 refs.

The authors record their results in the treatment with streptomycin of 93 patients with tuberculous meningitis at the Radcliffe Infirmary, Oxford, since November, 1946. In the first 60 cases, in which treatment started more than 1 year ago, the recovery rate was 50%. This favourable figure is attributed to the length of course employed, streptomycin being given intrathecally for the first 6 to 12 weeks or longer (adults 100 mg., infants and children 50 to 75 mg. daily) and intramuscularly without rest periods for at least 6 months (adults 2 g. daily, infants and children 20 mg. per lb. (9·1 mg. per kg.) body weight). A sanatorium routine for a further 3 to 6 months followed. In the survivors, intellectual recovery was good; total deafness occurred in 2 cases, fits in 1 (in a patient who had had epilepsy before the attack of meningitis), slight weakness in one hand in 2, and tuberculosis elsewhere in 4. As the results of treatment in patients in whom the meningitis was accompanied by miliary disease or adult-type pulmonary tuberculosis had been bad, such cases have been treated, since late 1948, with intramuscular streptomycin for 12 months and 3 or 4 courses intrathecally; the results so far have been good.

It is stressed that tuberculous inflammation of the meninges is slow to subside, even in the most favourable cases. Intrathecal administration of streptomycin should be prolonged for at least 8 weeks after the last positive films or cultures have been obtained, until fluctuations in the cell count of the cerebrospinal fluid have disappeared and its protein content is stationary or falling, and until there is no clinical evidence of active disease. Intramuscular treatment must continue for at least 180 days and until there has been steady improvement for at least 2 months. The authors state that streptomycin can never be given for too long a period, and that " there should never be a day during treatment when one does not have free access to the cerebro-spinal pathways ". For purposes of diagnosis and of specific and symptomatic treatment, the authors prefer to make bilateral frontal burr holes at the outset of treatment. In several cases polyethylene tubes were placed in the cisternae chiasmatica et interpeduncularis for the purpose of local application of the drug. In the small group of cases in which there is a strong suspicion, but no proof, of tuberculous meningitis, streptomycin should be given promptly. In most instances in which the diagnosis is correct, within a few days of the first intrathecal streptomycin injection there is a fluctuating rise in the fluid's content of cells and protein, whereas in non-tuberculous patients a fall is usual. In treated cases of miliary disease meningitis may evolve insidiously, so that lumbar puncture should be performed weekly.

The most interesting item in this report concerns the treatment of intractable cases (which constituted 40% of the series). Tuberculin (P.P.D.) in minute amounts was injected intrathecally into 3 patients " in whom all hope of recovery had been abandoned " during the course of streptomycin. Two made a very unexpected recovery and the third (who had decerebrate rigidity) improved, only to die later. In all there was an early intense clinical reaction and pleocytosis in the cerebrospinal fluid. It is claimed that these results " proved beyond reasonable doubt that the effect of the intrathecal injection of purified protein derivative is to dissolve the exudate ". Stress is laid on the need for extreme caution in the use of tuberculin in this way. *J. V. Hurford*

843. **The Significance of the Pathogenesis of Tuberculous Infection on the Course of Tuberculous Meningitis in Children after Streptomycin Treatment.** (De betekenis van de pathogenese der tuberculeuze infectie voor het beloop van meningitis tuberculosa bij kinderen na behandeling met streptomycine)

A. DE MINJER. *Maandschrift voor Kindergeneeskunde* [*Maandschr. Kindergeneesk.*] **18**, 285–323, 1950. 18 figs., 38 refs.

A necropsy study is presented of 11 cases of tuberculous meningitis at the Children's Hospital, Utrecht, in which combined intramuscular and intrathecal streptomycin therapy had been given.

Five children whose condition had not responded at all constitute a first series; they all died within a month of beginning treatment. In the 6 others, death did not occur for 2 to 5 months; they constitute a second series.

At necropsy signs of tuberculous meningitis were found in all cases, but only in the second series could a response to treatment be detected. In the first series an extensive primary complex, which on microscopical examination appeared to be recent, was demonstrated together with recent dissemination in other organs. In 3 cases the primary complex appeared to consist of multiple primary lesions; in the other 2 there was only one large lung lesion. In the second series small and calcified primary complexes were found, with healed, or nearly healed, foci of haematogenous dissemination.

Clinically, in the first series the primary infection, dissemination, and meningitis had developed in rapid

succession and in some cases practically simultaneously, but in the second series a considerable time had elapsed between primary infection and dissemination. In the first series mass infection was considered more probable, while the dissemination in the second series was considered to be more of an accidental nature. The author suggests that the difference in pathogenesis explains the difference in response in the two series.

Margaretha Adams

844. **Treatment of Tuberculous Meningitis with Streptomycin and Streptokinase in Combination.** (Kombinerad streptomycin- och strepto-kinasbehandling vid tuberkulos meingit)

P. HEDLUND, T. HOLME, A. LICHTENSTEIN, and C. LINGEN. *Nordisk Medicin* [*Nord. Med.*] **44**, 1310–1313, Aug. 18, 1950. 12 refs.

Spinal block is a frequent complication of tuberculous meningitis. To prevent this complication the authors utilized the fibrinolytic properties of streptokinase by administering it in 5 cases treated with streptomycin. In 2 of these cases signs of spinal block preceded the administration of streptokinase; in both of these the condition improved after treatment. In 3 further cases it was given as a preventive measure. In one of these no signs of block were demonstrated at any time; in the second one it was found coincidentally with the evidence of early blockage that the streptokinase used had lost its potency; after administration of a fresh solution the signs of block disappeared again and did not recur. The remaining case was one of relapse of tuberculous meningitis after apparent cure by treatment with streptomycin alone. During the second attack streptomycin and streptokinase were both administered from the beginning; blockage was never definitely demonstrated clinically, but the intracranial pressure increased and the patient died; necropsy revealed a spinal block of long standing. *W. G. Harding*

845. **Effects of Intrathecal Tuberculin and Streptomycin in Tuberculous Meningitis**

H. V. SMITH and R. L. VOLLUM. *Lancet* [*Lancet*] **2**, 275–286, Aug. 19, 1950. 19 figs., 20 refs.

The gross fluctuations in the cell count of the cerebrospinal fluid which frequently occur in the first few weeks of the treatment of tuberculous meningitis with streptomycin were investigated. Because such fluctuations are not seen in the later stages of treatment or in cases of non-tuberculous meningitis treated with streptomycin it was thought unlikely that the high cell counts were due to direct irritation by streptomycin given intrathecally. It seemed possible that the fluctuations might be due to release of tuberculin caused by the break-up of the bacterial cells. In confirmation, it was found that 0·75 to 7·5 μg. of purified protein derivative of tuberculin (P.P.D) injected intrathecally into 5 Mantoux-negative subjects gave rise to no clinical upset or significant change in the cell count or protein content of the cerebrospinal fluid. By contrast, when streptomycin was given in doses of 0·00375 to 3·75 μg. to subjects positive on intradermal testing to 0·1 ml. of 1 in 100 to 1 in 1,000 old tuberculin, there was always a brisk clinical and cellular response. The former consisted in fever and vomiting, maximal 12 to 24 hours after injection and subsiding in 2 to 3 days. The cell count rose to 300 to 3,000 cells per c. mm., with 30 to 80% polymorphonuclears on the first day. The count fell for the next 3 to 4 days and then usually rose again to a second peak, which was mainly lymphocytic. The protein content also rose to 80 to 400 mg. per 100 ml. and then slowly fell, though here also there might be a slight secondary rise. The cell count and protein levels then slowly fell, though it might be many weeks before they returned to normal.

In an attempt to demonstrate the presence of tuberculin in the cerebrospinal fluid, filtered fluid, taken from 4 patients at the height of the cellular disturbance, was injected intradermally into Mantoux-positive subjects. All the results were negative.

Finally the authors tried to reproduce the cellular fluctuations in 2 patients with tuberculous meningitis in whom streptomycin treatment had obviousy failed and who had passed beyond the stage when such fluctuations usually occurred. Both had reached the terminal hydrocephalic stage from which, on previous experience, recovery was not to be expected. Both cases responded to intrathecal P.P.D. with brisk meningeal reactions, clinical and cellular. To everyone's astonishment, after repeated P.P.D. injections the patients began to improve and at the time of reporting both seemed well on the way to recovery. P.P.D. was given intrathecally in a third case, in which a fully decerebrate state had developed. The illness was prolonged for 6 months and some improvement was observed. The patient finally died, and at necropsy none of the usual exudate was found surrounding the brain stem. It was thought that in all 3 cases such an exudate had been present but had resolved under the influence of combined streptomycin and P.P.D.

Seven other patients were having the combined treatment at the time of the report. Only one had died during the first 3 months of treatment. It is emphasized that intrathecal use of P.P.D. can be extremely dangerous, and it must be given only under the closest possible supervision. The following scheme is that in use at the time of the report: " On admission 0·1 ml. of 1 in 1,000 old tuberculin is injected intradermally. Then, as soon as the diagnosis is confirmed, bifrontal burr-holes are made. A standard solution of P.P.D. is made up containing 7·5 μg. per ml. and this is further diluted 10-fold, 100-fold, and 1,000-fold. If the Mantoux test is strongly positive, then 0·5 ml. of the 1,000-fold dilution is injected intrathecally and this is doubled every other day until a reaction is obtained. If the Mantoux test is weakly positive then 1·0 ml. of the 1,000-fold dilution is injected and the dose is at first trebled or even quadrupled every other day, depending on the strength of the Mantoux reaction. When we are giving 0·5 ml. of the 100-fold dilution we increase the dose more cautiously in order to avoid too severe a reaction. Once a reaction is obtained, either clinically or by a rise in cells, the same dose is repeated. From then on the size and timing of each dose is decided on according to the severity of the last reaction. On the whole it seemed wiser to give the injections every

third or fourth day so as to allow 2 or 3 days free from fever and vomiting. The dose is gradually increased as the patient becomes more tolerant of the injections."

[Although these results are only preliminary, the combination of streptomycin and tuberculin may well represent an important advance in the treatment of tuberculous meningitis and possibly of other forms of tuberculosis. But it is clear that it is potentially dangerous and at present only to be used under experienced supervision and in carefully selected cases.]

John Crofton

846. **Laryngeal Tuberculosis and the Effect of Streptomycin Treatment.** (Gruźlica krtani ze szczególnym uwzględnienium wyników leczenia streptomycyną)
T. OBTUŁOWICZ. *Gruźlica* [*Gruźlica*] **18**, 102–117, Jan.–March, 1950. 1 fig., 7 refs.

For treatment of laryngeal tuberculosis (of infiltrative or ulcerative type) 0·25 to 0·5 g. of streptomycin daily in two doses a day for 30 days suffices, unless the presence of lung lesions calls for a higher dosage. If after this time the laryngeal lesions are not subsiding and the tubercle bacilli show no increase in resistance to the antibiotic, the treatment should be continued.

The best results are achieved in the treatment of haematogenous tuberculosis of the larynx, in cases of fresh infiltration and ulceration showing no hypertrophic changes, and in the oedematous form, providing that the pulmonary tuberculous lesions are recent or only moderately advanced. For old hypertrophic lesions the author recommends combined treatment by administration of streptomycin and cauterization. His observations are based on 201 cases of laryngeal tuberculosis as a complication of pulmonary tuberculosis; 87 patients recovered and in 57 the condition improved, but no change, or worsening of the condition, was observed in 38 cases (19 cases were not followed up).

J. W. Czekalowski

847. **Tuberculosis of the Trachea and Bronchi.** (La tuberculosis de la traquea y de los bronquios)
I. F. WOLAJ, J. VERGALLO YOFRE, R. D. EVANGELISTA, M. GÓMEZ CASCO, and J. OSTROVSKY. *Prensa Médica Argentina* [*Prensa méd. argent.*] **37**, 2176–2181, Sept. 15, 1950. 6 figs.

Tracheo-bronchial tuberculosis is a frequent complication of pulmonary tuberculosis and may appear at any stage in the disease.

This account is based on the findings in 37 cases (9·9% of the total number of tuberculous patients). Age and sex do not appear to be of significance in the incidence. A definite endobronchial lesion was found in 27 cases, in 2 cases as a result of a primary infection and in 25 cases as a consequence of re-infection. Advanced lesions of the re-infection type appear to be the commonest antecedent to bronchial disease. The presence of persistent cough, wheezing, and dyspnoea indicate the presence of bronchial disease. Radiologically, tension cavities and atelectasis have a similar significance. The presence of this complication introduces a hazard in artificial pneumothorax treatment, and in 62·5% of the cases the result of this treatment was unsuccessful. Thoracoplasty is the treatment of choice.

Streptomycin appears to improve the symptoms of bronchial tuberculosis, but there was no marked difference in the endoscopic appearances in two groups of cases treated by local applications of silver nitrate with and without streptomycin respectively. *J. J. Giraldi*

848. **Aerosol Streptomycin Treatment of Advanced Pulmonary Tuberculosis in Children**
J. B. MILLER, H. A. ABRAMSON, and B. RATNER. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **80**, 207–237, Aug., 1950. 11 figs., bibliography.

Experiences are described in the treatment of advanced pulmonary tuberculosis with aerosol streptomycin in 12 children. Careful attention was paid to technique, special inhalers and face hoods being devised; a large dose of streptomycin, 2 g. daily, made up in an alkaline solution with " triton A-20 ", a detergent, was used for periods of 3 to 6 months. Very satisfactory responses were obtained in 9 cases of cavitation and infiltration, but in the remaining 3 patients atelectatic lesions due to enlarged hilar lymph nodes were not influenced by the treatment. *Winston Turner*

849. **The Chemotherapy of Tuberculosis with " Conteben " (*p*-Acetaminobenzaldehyde Thiosemicarbazone) and *p*-Aminosalicylic Acid.** (Die Chemotherapie der Tuberkulose mit Conteben und PAS)
H. FRAHM. *Zeitschrift für Tuberkulose* [*Z. Tuberk.*] **96**, 5–14, 1950. 29 refs.

The thiosemicarbazone of *p*-acetaminobenzaldehyde (" conteben " or thiacetazone) acts exclusively on *Mycobacterium tuberculosis*. The specific bacteriostatic effect *in vitro* is exerted between concentrations of 1 in 5,000 to 1 in 10,000 and 1 in 100,000 to 1 in 250,000. The individual tolerance varies considerably. Of tested individuals 60% state that the drug has a bitter taste and 40% that it is tasteless. Nausea and vomiting, two of the observed side-effects, may affect the taste reaction. Estimations of concentration in blood after different doses show that a daily dose of less than 0·1 g. cannot be expected [in theory] to have any bacteriostatic effect. No standard scheme of dosage can be given, but gradual increase from a low starting level of 0·025 g. is recommended. In more than one-third of an observation group, anaemia developed with doses of 0·15 g. per day. In a few cases this anaemia persists and the dose has to be reduced. Leucocytosis is usual, monocytosis is sometimes observed, the thrombocyte count usually remains normal. One case of " allergic " agranulocytosis was observed in 89 patients. Liver damage is a common side-effect. Severe headache due to cerebral oedema has been noted. A marked fall in erythrocyte sedimentation rate during treatment is characteristic of the effect of the drug on serum proteins and not on the disease process, for the latter may remain unchanged in spite of serological " improvement ". The effect of the drug is believed to be partly due to a non-specific action on the autonomic nervous system, this being as important as the specific bacteriostatic action. The tuberculin reac-

tion weakens; this points to an anti-inflammatory effect of the drug, as does its beneficial effect in chronic arthritis. Though a daily maximum dose of 0·3 g. is tolerated by some persons it is not advisable to give more than 0·15 g. a day in 3 doses of 0·05 g. at 4- to 6-hour intervals.

Summarizing the published reports on the treatment of pulmonary tuberculosis, the author observes that results vary between complete failure and success. Heilmeyer found marked to moderate improvement in 50% of cases, particularly in cases of fresh infiltration and fresh aspiration foci. Only after treatment for several months can good results be expected. Prolongation of treatment depends on individual tolerance.

Non-pulmonary lesions, particularly intestinal and laryngeal ones, respond well (more so to local application). Tuberculosis of the skin reacts very favourably to high doses. [Calciferol would be a less dangerous drug.] With sinuses complicating skeletal tuberculosis excellent results are obtained. Whereas the combination of this drug with streptomycin gave results no better than with either of the drugs alone, combination with *p*-aminosalicylic acid appears to have a cumulative effect. This may be the combination of choice whenever the thiacetazone is indicated.

[Considering the high toxicity of, and limited tolerance to, thiacetazone, the action of which is partly non-specific, it is questionable whether there is a great field for this new "wonder-drug"—with or without *p*-aminosalicylate.] *E. G. W. Hoffstaedt*

850. **Acquired Idiosyncrasy to Sodium *p*-Aminosalicylate**
J. CUTHBERT. *Lancet* [*Lancet*] **2**, 209–211, Aug. 5, 1950. 1 fig., 6 refs.

A patient with pulmonary tuberculosis developed a severe pyrexial illness, associated with an extensive maculo-papular rash, adenopathy, anuria, and jaundice, during a course of treatment with sodium *p*-aminosalicylate (PAS). That the illness represented an idiosyncrasy to PAS was suggested by a positive skin reaction to a "patch" impregnated with PAS, a favourable response to antihistamine drugs, effective desensitization with PAS during convalescence, and negative laboratory reactions for other diseases which produce a similar clinical picture.

The toxic reaction began suddenly after the drug had been given in a dose of 20 g. daily for approximately one month. [Three cases of hypersensitivity to PAS, with clinical features similar to those reported above, are described in *Lancet*, 1950, **2**, 308.] *G. B. Forbes*

851. **The Use of PAS in the Treatment of Draining Tuberculous Empyemata**
M. R. LICHTENSTEIN and P. ALFANO. *Diseases of the Chest* [*Dis. Chest*] **18**, 93–97, Aug., 1950. 2 refs.

The effect of *p*-aminosalicylic acid (PAS) was studied in a controlled series of 22 patients with discharging tuberculous empyemata, all of whom had undergone thoracotomy. Eleven patients received the sodium salt (NaPAS), 3 g. four times a day orally for 120 days, while 11 patients matched as controls as closely as possible received a placebo. After 60 days of this regimen, 4 patients in each group were treated twice daily with 5% NaPAS packs in the wounds for the last 60 days of the experiment. Saline packs were used as controls. Clinical effects were assessed in terms of general condition, cough, quantity of sputum, fever, and alteration in weight. Smears and cultures of the pus were studied every 2 months, blood PAS levels once every month; PAS level was determined in pus once, while the patient was on oral therapy alone. In those patients without broncho-pleural fistulae the size of the empyema space was estimated from the amount of saline required to fill it.

The therapy produced no significant improvement. In 5 patients receiving the drug by mouth the level in the pus averaged 1 mg. per 100 ml.: in 5 other patients no drug was found in the pus. The wounds in cases treated with local PAS packs were cleaner than the untreated wounds, and there was some diminution in amount, with thinning, of the pus in the same group. [This was probably due to the reduction in secondary infection.] *Kenneth Marsh*

852. **The Final Stages of Aspiration-drainage of Tuberculous Cavities.** (Die Kavernensaugdrainage in ihrer Endphase)
V. MONALDI and F. DE MARCO. *Münchener Medizinische Wochenschrift* [*Münch. med. Wschr.*] **92**, 823–826, Sept. 1, 1950. 3 figs.

853. **A Critical Survey of the Erythrocyte Sedimentation Rate, Lability Reactions, and Differential Blood Count in Pulmonary Tuberculosis.** (Kritische Betrachtung von Blutkörperchensenkung, Labilitätsreaktionen und Differentialblutbild bei der Lungentuberkulose)
H. FUCHS. *Zeitschrift für Tuberkulose* [*Z. Tuberk.*] **96**, 41–48, 1950. 44 refs.

A rise in erythrocyte sedimentation rate (E.S.R.) implies essentially an increase in plasma globulins. The E.S.R. depends, apart from the total erythrocyte volume, on chemical factors, that is, on the plasma colloids necessary and responsible for rouleaux formation. The observed discrepancies between the E.S.R. and the actual disease condition may be due to various factors interfering with the plasma colloid stability or with rouleaux formation. Thus sedimentation may be retarded rather than accelerated. Liver damage, hyperthyroidism, and disturbances in the diencephalon are some of the delaying factors mentioned.

[Retardation of sedimentation in various conditions, such as neurosis, allergic diseases, peptic ulcer, and hyperthyroidism, has been previously described by the abstracter (*Dtsch. med. Wschr.*, 1928, **54**, 1925; *Med. Klin.*, 1931, **27**, 52).] The E.S.R. often "lags behind" and response to intercurrent infection has nothing to do with the underlying disease. Thiosemicarbazone usually rapidly "improves" the E.S.R. without always improving the lung condition. Quite a number of patients with active tuberculosis, particularly if the latter is developing slowly, may have a normal E.S.R. Cases are known of perfectly healthy persons with a raised E.S.R. for years. Various modifications of technique have not

improved the test much, but have made comparisons impossible. A number of other serological "lability reactions", such as the Weltmann coagulation-band method, the formol-gel reaction, and the Takata reaction, do not give better results. Costa's protein-flocculation reaction (with procaine and formalin solution and citrated blood) has given more promising and reliable results. [For details see the original. The author did not employ the cadmium sulphate test, which is only mentioned as a possibility.] The differential leucocyte count is of value and is used in conjunction with the E.S.R. and the Costa reaction. By comparison of results in these three tests the author found, in a series of 340 patients, agreement of results with the actual disease condition in 46·5%. In 18% the result of the Costa reaction did not correspond to the pathological condition. In 35%, however, the Costa reaction was found to be more reliable, and to reflect more accurately than the E.S.R. and/or the blood count the actual state of affairs.

As long as the limitations and the sources of error of E.S.R. measurements are kept in mind, this simple method will remain a useful help in day-to-day assessments of progress in tuberculosis, particularly if this test is supplemented by differential leucocyte counts and the Costa reaction. *E. G. W. Hoffstaedt*

854. **Significance of Examination for Tubercle Bacilli in Stomach and Bronchial Washings.** (Значение исследования на туб. бациллы промывных вод желудка и бронхов)
M. S. Rozenblat, E. R. Krichevskaja, and B. F. Bruk. Проблемы Туберкулеза [*Probl. Tuberk.*] No. 3, 9–12, May–June, 1950.

Bronchial and stomach washings from patients with pulmonary tuberculosis were examined for the presence of tubercle bacilli. The bronchial washings were obtained by cocainizing the fauces and injecting 20 ml. of saline through the larynx with a syringe and catheter; the fluid was returned by the coughing which resulted. Out of 116 patients tubercle bacilli were found in washings from both sources in 23 cases (20%); they were absent from both washings in 78 cases (67%). The agreement between the results by the two methods indicates that the bacilli which are found in the stomach are derived from the bronchi. In 6% of the cases tubercle bacilli were found in sputum smears as well as in bronchial and stomach washings. No adverse effects followed the injection of fluid into the bronchi, and the method is of use for investigating cases in which examination of the sputum gives negative results. *D. J. Bauer*

855. **Excretion of Acid-fast Bacilli in the Absence of Tuberculous Changes in the Lungs.** (О выделении кислотоупорных бацилл при отсутствии выраженных туберкулезных изменений в легких)
T. N. Oleneva. Проблемы Туберкулеза [*Probl. Tuberk.*] No. 3, 13–19, May–June, 1950. 4 figs., 16 refs.

The discovery of acid-fast bacilli in sputum and stomach washings in the absence of visible radiological changes poses a difficult problem in diagnosis and treatment. It has been held that the bacilli arise from lesions which are too small to be detectable, but there is also the possibility that they might be non-pathogenic acid-fast organisms ingested with food. The author describes a series of 34 cases of various lung conditions in which there was no radiological evidence of tuberculosis. Examination of the sputum revealed the presence of acid-fast bacilli in 28 cases, and similar organisms were found in stomach washings in 4 cases. They could be cultured only with difficulty, were non-pathogenic for guinea-pigs, and were usually found only once in repeated examinations. By observation over a long period the correct diagnoses were shown to be chronic bronchitis, interstitial pneumonia, bronchiectasis, lung abscess, and bronchial carcinoma; pulmonary tuberculosis developed in one case only. *D. J. Bauer*

856. **The Effect of Penicillin and Some Other Antibiotics on Tubercle Bacilli.** (О действии пенициллина и некоторых антибиотиков на туберкулезные бациллы)
V. N. Kosmodamianskii. Проблемы Туберкулеза [*Probl. Tuberk.*] No. 3, 20–26, May–June, 1950. 4 figs., 16 refs.

The effect of penicillin upon the growth of tubercle bacilli was investigated and compared with that of a filtrate of a culture of *Pseudomonas aeruginosa*. Russian and Canadian samples of penicillin were used, together with a filtrate of a 10-day culture of *Ps. aeruginosa*. Tubercle bacilli were added to solutions of penicillin containing from 32 to 15,000 units per ml. and incubated at 37° C.; morphological and cultural characteristics were examined at intervals. After 4 days non-acid-fast granules and Gram-positive cocci were seen; subculture after 8 days yielded colonies of non-acid-fast organisms. Similar effects were obtained both with penicillin and with the filtrate; a bacteriostatic effect was noted with the higher concentrations of penicillin. The non-acid-fast organisms which resulted from this treatment were pathogenic for rabbits; the reaction produced, however, was not typical of tuberculosis, but consisted of a chronic infiltration of lungs and spleen with lymphocytes and elongated cells of epithelial type. The organisms persisted in the tissues and could be recovered by passage after several months. *D. J. Bauer*

See also Section Hygiene and Public Health, Abstract 442.

PROTOZOAL INFECTIONS

857. **A Heretofore Unreported Agglutinable Human Blood Factor and its Possible Relationship to Blackwater Fever**
D. C. A. Butts. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **30**, 663–667, Sept., 1950. 4 refs.

It has previously been suggested that persons lacking the Rh agglutinogen might on exposure to repeated attacks of falciparum malaria develop a haemoagglutinin in sufficient concentration to bring about destruction of the parasitized erythrocytes. Subsequent observations

in Cuba and Guatemala on recovered cases of blackwater fever showed that this condition may develop in either Rh-negative or Rh-positive individuals. A new human agglutinable blood factor (Ch-haemoagglutinogen) has now been demonstrated by the use of chimpanzee-immune serum developed in rabbits. It is present in 97% of all healthy white group-O individuals and 97·4% of all healthy group-O negroes, thus strongly suggesting that it is not associated with the AB, MN, Rh-Hr, or P systems. It is possible that this factor may explain unaccountable reactions following the transfusion of "compatible" blood. The hypothesis is put forward that malaria parasites, especially *Plasmodium falciparum*, possess a relatively strong Ch-like agglutinogen. If individuals lacking the Ch-haemoagglutinogen are exposed to repeated re-infections with *P. falciparum* (antigen), it is thought that in time they may in time develop an "anti-Ch agglutinin" (antibody) in sufficient amount to bring about the agglutination of parasitized cells. Quinine by causing the spleen, the storehouse of the haemoagglutinin, to contract would release the anti-Ch agglutinin in sufficient concentration to cause agglutination and subsequent haemolysis of parasitized cells.

G. M. Findlay

858. **N^1-3 : 4-Dichlorophenyl-N^5-*iso*propyl Diguanide—a Derivative of Proguanil Highly Active in Avian Malaria**
F. H. S. Curd, D. G. Davey, J. A. Hendry, and F. L. Rose. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **15**, 438–444, Sept., 1950. 3 refs.

Tests were made of the antimalarial activity and toxicity of N^1-3 : 4-dichlorophenyl-N^5-*iso*propyl diguanide (M5943), which differs in chemical structure from proguanil ("paludrine") only in having an extra chlorine atom in position 3 of the benzene ring; it was chosen from a number of such compounds with dihalogen substitution in positions 3 and 4 of the benzene ring, a substitution found to be very favourable for antimalarial activity. Its action on *Plasmodium gallinaceum* in 6-day-old chicks and *P. relictum* in canaries was tested, and its toxicity was assessed on chicks, mice, rats, dogs, and monkeys. During the last 2 years it has been tried in human malaria in England and Calcutta and reports of these trials will probably soon be published. It is a white crystalline powder with a solubility in water of about 1 g. in 100 ml., and solutions may be boiled.

The tests are described and shown in tables; chicks and canaries were injected intravenously with sporozoites for tests of activity against exoerythrocytic parasites and with infected erythrocytes to test its activity against these forms. The drug was given orally.

M5943 is much more active than proguanil against both the blood forms and the exoerythrocytic forms of *P. gallinaceum* and *P. relictum*; complete protection was obtained in most of the birds when treatment was begun a few hours after the injection of sporozoites, and blood infections were controlled but not cured. The drug is about as toxic as proguanil to mice and rats but is more toxic than proguanil to chicks, dogs, and monkeys; because of this toxicity and of its similarity to proguanil the authors do not expect that M5943 will have better effects in human malaria than proguanil, but a more precise judgment awaits the results of the trials in man [see also these *Abstracts*, 1948, **3**, 555]. *J. F. Corson*

859. **Treatment of Kala-azar with Methyl Glucamine Antimoniate**
P. C. Sen Gupta. *Indian Medical Gazette* [*Indian med. Gaz.*] **85**, 291–296, July, 1950. 15 refs.

A series of 24 Indian patients suffering from kala-azar were treated in Calcutta with methyl glucamine antimoniate. Nineteen were admitted to hospital and given intramuscular injections on alternate days, the dosage varying in different cases. A 30% solution was used, the maximum single dose being 15 ml. for adults and 5 to 7·5 ml. for young children. The total amount administered to patients who responded ranged from 87·5 to 215 ml. (mean 165·6 ml.) for adults, and 82·5 to 145 ml. (mean 113 ml.) for children. The mean relative total dose was 181·4 ml. per 100 lb. body weight (4 ml. per kg.) for adults, and 319·8 ml. per 100 lb. (7·05 ml. per kg.) for children. The toxicity of the drug was very low.

The disease in 5 of the 19 in-patients had previously proved drug-resistant: 3 of these resistant cases and the other 14 (previously untreated) cases responded well. Of 11 cases followed up after 6 months only one had relapsed.

Five patients were treated as out-patients with methyl glucamine antimoniate given in twice-weekly injections. The immediate response was good, but the relapse rate is not yet known.

The diagnosis of the cases was made mostly by identification of the parasite in either splenic or bone-marrow smears, but in some cases it rested on a positive result with Napier's aldehyde test. Detailed case-histories are given. *W. H. Horner Andrews*

860. **The Chemotherapeutic Action of Phenanthridine Compounds. Part IV. Activity *in vitro***
J. A. Lock. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **5**, 398–408, Sept., 1950. 6 figs., 4 refs.

To gain information on the mode of action of certain phenanthridine compounds on trypanosomes, investigations were carried out *in vitro* with the blood forms of *Trypanosoma rhodesiense* and *T. cruzi*. Though dimidium bromide (2 : 7-diamino-9-phenyl-10-methylphenanthridinium bromide) is relatively more active *in vivo* against *T. congolense* than against *T. rhodesiense*, it was not possible to carry out studies *in vitro* with *T. congolense* because a satisfactory growth could not be obtained with this trypanosome; consequently *T. rhodesiense* alone was used in testing this drug. The trimidium compound (2 : 7-diamino-9-*p*-aminophenyl-10-methylphenanthridinium chloride), which is 1·5 times as active as dimidium *in vivo* against *T. congolense* and 4 times as active against *T. rhodesiense*, was found *in vitro* to kill 90% of *T. rhodesiense* at a dilution of 1 in 1,000,000, which was the same figure as for dimidium. The compound 7-carbethoxyamino-9 : 10-dimethylphenanthridinium bromide, which is relatively inactive *in vivo* against *T. rhodesiense*, killed the trypanosomes *in vitro* at a dilution of 1 in

250,000. Thus considerable activity may be displayed *in vitro* by a compound which is relatively inactive *in vivo*. These phenanthridinium compounds exerted a direct trypanocidal action *in vitro*, and brief exposure to an effective drug either *in vitro* or *in vivo* appreciably affected the power of survival of both *T. rhodesiense* and *T. congolense*, but there was no appreciable absorption of the drugs by living trypanosomes, nor could any activation of the drugs *in vivo* or *in vitro* be detected.

Many of the compounds tested were found to be active against *T. cruzi in vitro* in dilutions similar to those effective against *T. rhodesiense*. Dimidium bromide was also shown to have a direct toxic effect on the extracellular forms of *T. cruzi* in tissue culture.

R. Wien

861. **Parasitology, Pathology, and Serology of Fatal Toxoplasmosis.** (Zur Parasitologie, Pathologie und Serologie tödlicher Infektionen mit *Toxoplasma gondii*)
G. PIEKARSKI and H. v. TÖRNE. *Klinische Wochenschrift* [*Klin. Wschr.*] **28**, 606–609, Sept. 15, 1950. 5 figs., 10 refs.

This is a report of 2 fatal cases of toxoplasmosis in infants. In the first child the parasites were found in the form of the so-called pseudocysts in the brain and retina. Other organs were not examined, as the disease was not diagnosed before death and for the same reason no serological tests were made. In the second case the diagnosis was made before death and neutralizing antibodies were found in the blood of the infant and the mother. Parasites were found only in the lungs and kidneys, and there only with difficulty. In neither case were there any intracerebral foci of calcification. Two tests for the presence of antibodies in the serum are described in detail. *Marianna Clark*

OTHER INFECTIONS

862. **Complications of Q Fever.** (Komplikationen des Q-fever)
S. MOESCHLIN and B. J. KOSZEWSKI. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **80**, 929–931, Sept. 2, 1950. 4 figs., 13 refs.

Among 50 patients in whom a diagnosis of Q fever was established clinically and serologically there were 9 with complications not involving the lungs. Five patients suffered from thrombophlebitis and pulmonary embolism, 3 from epididymitis, 1 from acute pancreatitis, and 1 from encephalitis. Of 9 patients with meningeal symptoms only 1 had an increased number of cells in the cerebrospinal fluid. All these extrapulmonary complications occurred after the remission of the lung symptoms, between the 14th and 23rd days in the case of thrombophlebitis, on the 18th day in the case of encephalitis, and between the 26th and 43rd days in cases of epididymitis and pancreatitis. That these late complications are due to the action of rickettsiae is not absolutely proved, but in one patient with epididymitis 5 weeks after the onset of Q fever inoculation of urine into a guinea-pig showed that rickettsiae were still present. Since these severe complications are by no means rare it is urged that all patients who have suffered from Q fever should be kept under medical observation during convalescence and should not be allowed to return to work for at least 3 to 4 weeks after the temperature has become normal. *G. M. Findlay*

863. **Treatment of Rickettsialpox with Aureomycin**
H. M. ROSE, Y. KNEELAND, and C. D. GIBSON. *American Journal of Medicine* [*Amer. J. Med.*] **9**, 300–307, Sept., 1950. 8 figs., 20 refs.

Aureomycin is known to be a potent antirickettsial agent, consistently effective in Rocky Mountain spotted fever, tick-bite fever, typhus, scrub typhus, Brill's disease, and Q fever. This study reports the prompt response to aureomycin of 8 cases of rickettsialpox, an infection due to *Rickettsia akari* and endemic in New York City. Its clinical manifestations and laboratory diagnosis have been described earlier (Rose, *Ann. intern. Med.*, 1949, **31**, 871). *Henry Cohen*

864. **Studies on the Life Cycle of Spirochetes. III. The Life Cycle of the Nichols Pathogenic *Treponema pallidum* in the Rabbit Testis as Seen by Phase Contrast Microscopy**
E. D. DELAMATER, R. H. WIGGALL, and M. HAANES. *Journal of Experimental Medicine* [*J. exp. Med.*] **92**, 239–246, Sept., 1950. 14 figs., 6 refs.

865. **Studies on the Life Cycle of Spirochetes. IV. The Life Cycle of the Nichols Pathogenic *Treponema pallidum* in the Rabbit Testis as Visualized by Means of Stained Smears**
E. D. DELAMATER, R. H. WIGGALL, and M. HAANES. *Journal of Experimental Medicine* [*J. exp. Med.*] **92**, 247–252, Sept., 1950. 3 figs., 8 refs.

These two papers form part of a series of articles on the life cycle of strains of *Treponema pallidum* [of the five papers indicated in the list of references only one has yet been published]. The observations recorded in the present papers are concerned with phase-contrast microscopy of the living organism and the microscopic appearance of the same strain of treponeme as that seen in stained-smear preparations. This particular strain, the " Nichols pathogenic *T. pallidum* " is pathogenic for rabbits, and the material for the observations was obtained from experimental testicular cultures.

In most instances the organism appeared to be coiled as a spiral with a round transverse cross-section. On occasions organisms were seen which appeared as a flat rather than a coiled spiral. In freshly prepared specimens there was active movement consisting of the well-known rotary motion with occasional undulations, and also bending, twisting, and lashing movements. The latter were frequently seen as a prelude to transverse fission, when the two parts seemed to break away from each other where the bending was most acute. In a small proportion bodies, having the appearance of gemmae or buds, were noted in either a medial position or a terminal position. The observations suggest that these buds can be thrown off from the spiral form and become free, and that an asexual development cycle then takes place

within the bud or cyst from which eventually a number of young spiral forms may emerge.

Further observations suggest that, after conjugation of two or more spiral forms at about their middle third, a somewhat larger, complex developmental cyst may form in which organisms can develop and finally emerge as a tangled mass of threads, to take on typical spiral forms which later divide transversely in the usual manner.

In a series of well-reproduced photographs of the phase-contrast microscope preparations and the ordinary stained smears, most of the stages described in the text can be followed. The authors are cautious in their suggestions as regards this complex life cycle. They indicate that further investigations are in progress and that subsequent papers will deal in more detail with some of the processes involved. *H. J. Bensted*

866. **Leptospirosis of the Eyes. (לפטוספירוסיס בעיניים)**
S. KANNER. *Harefuah* [*Harefuah*] **38**, 158, May 15, 1950.

Nearly 100 cases of ocular leptospirosis were observed. Ocular signs of diagnostic value, which appear on the first day, include pronounced bulbar, conjunctival, or mixed ciliary injection, and sometimes subconjunctival haemorrhages. Retinal haemorrhages may also occur. The initial signs disappear in a few days to be followed by iridocyclitis at any time after the second week after the general illness has run its course (even after a period of months). All patients recovered completely, though there is no specific treatment. None of the antibiotics had any effect. *A. Feigenbaum*

867. **Treatment of Acute Rheumatism with Sodium Gentisate.** (Prime ricerche cliniche sulla terapia del reumatismo articolare acuto col gentisato sodico)
F. TESTONI and A. STRANO. *Minerva Medica* [*Minerva med., Torino*] **2**, 450–456, Sept. 15, 1950. 5 figs., 6 refs.

Because of the toxicity of salicylates a search is being made for compounds which have the same therapeutic actions without the side-effects. The latest to be tried is sodium gentisate, which is the sodium salt of 2 : 5-dihydroxybenzoic acid, a substance normally found in the urine of patients treated with salicylates.

Seven patients were treated with this drug in the Medical Unit of the University of Catania, and a preliminary report of their progress is presented. Five of these were young people with typical "rheumatic" histories and evidence of joint and heart involvement, the latter often of severe degree; the 2 other patients were older and were suffering from a generalized arthritis. The majority had already had some treatment with salicylates, with poor results. However, soon after treatment with 15 to 25 g. sodium gentisate daily by mouth in divided doses began (in the most severe cases smaller doses were given intravenously in addition), there was marked clinical improvement, even in patients with cardiac failure. More important is the fact that, even with such large doses, only one case showed signs of toxicity and these were not severe. The effect on the erythrocyte sedimentation rate was not marked, and the slow fall in this rate was unrelated to the dramatic improvement produced by the drug.

The compound has no direct antipyretic action, but is a weak analgesic and a definite diaphoretic. A comparison with salicylates shows that the latter are more active therapeutically; a point of some interest is that salicylates appear to be more effective in cases treated with gentisate. *A. Paton*

868. **Relationship of Bone Marrow Plasmacytosis to the Changes in Serum Gamma Globulin in Rheumatic Fever**
R. A. GOOD and B. CAMPBELL. *American Journal of Medicine* [*Amer. J. Med.*] **9**, 330–342, Sept., 1950. 7 figs., bibliography.

Sternal-marrow biopsy material was examined and serum γ-globulin levels (estimated by Kunkel's $ZnSO_4$ turbidimetric method) were determined in 12 normal children, 22 with rheumatic fever, 15 convalescent from rheumatic fever, 6 with inactive rheumatic fever, 8 with acute Sydenham's chorea, 6 convalescent from chorea, 6 with acute streptococcal pharyngitis, and 3 convalescent from this disease. The findings show that in acute rheumatic fever plasmacytosis of the bone marrow is constant during the active phase (8 to 10 times the normal number of plasmacytes being found) and gradually diminishes with the subsidence of active signs. This plasmacytosis is significantly correlated with the plasma level of γ globulin. A similar, but slighter, change is found in patients convalescent from streptococcal pharyngitis. In chorea and inactive rheumatic fever the number of bone-marrow plasmacytes and the serum γ-globulin levels were normal. The relation between plasmacytosis and antibody production is discussed. [Elsewhere in the same issue of this journal Barr discusses the function of the plasma cell.] *Henry Cohen*

See also Section Pathology, Abstracts 558, 563.

869. **Infectious Mononucleosis with Hepatitis**
H. D. BENNETT, J. J. FRANKEL, P. BEDINGER, and L. A. BAKER. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 391–401, Sept., 1950. 30 refs.

Infectious mononucleosis occurs in three forms, namely, the glandular type, the type with severe infection of the pharynx and tonsils, and a type with general systemic febrile illness associated with widespread disability and frequently with obscure visceral symptoms. A series of 90 patients with this disease underwent the usual number of tests of liver function; the great majority were found to have either frank jaundice or demonstrable hepatitis, with considerable inefficiency of hepatic function. Clinicians should remember that every patient with glandular fever very probably also has hepatitis. *G. F. Walker*

870. **Infectious Mononucleosis: Report of a Case with Autopsy**
M. E. SHARP. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **62**, 175–187, April, 1950. 12 figs., bibliography.

See also Section Cardiovascular Disorders, Abstract 653.

History of Medicine

871. **Infant Feeding-bottles in Prehistoric Times**
A. D. LACAILLE. *Proceedings of the Royal Society of Medicine* [*Proc. R. Soc. Med.*] **43**, 565–568, July, 1950. 5 figs., 9 refs.

872. **Ancient Egypt and the Origin of Anatomical Science**
A. J. E. CAVE. *Proceedings of the Royal Society of Medicine* [*Proc. R. Soc. Med.*] **43**, 568–571, July, 1950.

873. **Origin of Syphilis.** (La invasion de la sifilis)
S. LAZO GARCIA. *Actas Dermo-sifiliográficas* [*Act. dermo-sifiliogr., Madr.*] **41**, 775–783, May, 1950.

874. **Russian Obstetric Forceps.** (Отечественные прямые акушерские щипцы)
K. N. ZHMAKIN. Акушерство и Гинекология [*Akush. Ginek.*] No. 3, 12–17, May–June, 1950. 5 figs., 1 ref.

875. **The History of Pharmacy in Catalonia.** (Contribucion al estudio de la historia de la farmacia en Cataluña)
J. ISAMAT VILA. *Anales de Medicina y Cirugia* [*An. Med. Cirug.*] **28**, 1–31, July, 1950. 1 fig., bibliography.

876. **How the Malaria Service in Indonesia Came into Being, 1898–1948**
N. H. SWELLENGREBEL. *Journal of Hygiene* [*J. Hyg., Camb.*] **48**, 146–157, June, 1950.

877. **The Death of President Garfield**
S. A. FISH. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **24**, 378–392, July–Aug., 1950. 2 figs., 19 refs.

878. **The Salpêtrière School: J. M. Charcot, Psycho-physiologist.** (L'école de la Salpêtrière: J. M. Charcot, psycho-physiologiste)
J. LHERMITTE. *Encéphale* [*Encéphale*] **39**, 297–310, 1950.

In 1848, when Charcot was a young student, little was known of diseases of the nervous system, and even the vital role of the cerebral cortex was still to be defined. Charcot possessed the gifts necessary to establish the new clinical specialty. His early interest in painting sharpened his naturally keen powers of observation, and his rapid sketches of pathological appearances proved a powerful aid to his retentive memory.

In 1862, at the age of 37, he returned to the Salpêtrière as chief physician and began his great work on hysteria. He soon refuted the accepted opinion that hysteria was confined to females; he described hysterotraumatic paralysis, notably brachial monoplegia, and followed this with a study of hysterical coxalgia. Much of this work has been amended and expanded by others, but he laid down the basic laws. Although sometimes deceived, Charcot knew as well as most the shrewd tricks, the lies, and play-acting to which certain hysterics are prone, and he himself warned against this simulation. He was aware of the influence of suggestion in hysterical manifestations and their cure, and he realized the need for isolation, especially in such grave states as hysterical anorexia.

The numerous cases of "shell-shock" in the first world war gave a great impetus to Charcot's teaching. Henri Claude built on the foundations laid down by his master when he demonstrated the association between hysteria and schizophrenia; he also confirmed Charcot's pioneer experiments which showed that, though ether often relieves hysterical contractions, chloroform does not, thus providing an objective guide to diagnosis. Charcot's experiences with patients who had undergone amputation and had phantom-limb sensations led him to stress the importance of investigating sleep states, dreams, and somnambulism. His descriptions of aphasia and visual agnosia are classics. All his work showed that there were true psychoneuroses without accompanying lesions of the nervous system and that these obeyed fixed laws and could therefore be understood and treated; the most important and the commonest of these conditions was hysteria. *F. N. L. Poynter*

879. **The Life and Work of Carlos Chagas.** (A vide e a obra de Carlos Chagas)
Arquivos de Cirurgia Clínica e Experimental [*Arch. Cirurg. clin. exp.*] **13**, 146–160, March–April, 1950. 1 fig., 14 refs.

880. **Thomas Harris, M.D., Naval Surgeon and Founder of the First School of Naval Medicine in the New World**
L. H. RODDIS. *Journal of the History of Medicine and Allied Sciences* [*J. Hist. Med.*] **5**, 236–250, Summer, 1950. 1 fig., 5 refs.

881. **John Snow, Pioneer Specialist-anaesthetist**
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